

Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management

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OBJECTIVE. The objective of our study was to determine the misdiagnosis rate of radiologists for coronavirus disease 2019 (COVID-19) and evaluate the performance of chest CT in the diagnosis and management of COVID-19. The CT features of COVID-19 are reported and compared with the CT features of other viruses to familiarize radiologists with possible CT patterns.

MATERIALS AND METHODS. This study included the first 51 patients with a diagnosis of COVID-19 infection confirmed by nucleic acid testing (23 women and 28 men; age range, 26–83 years) and two patients with adenovirus (one woman and one man; ages, 58 and 66 years). We reviewed the clinical information, CT images, and corresponding image reports of these 53 patients. The CT images included images from 99 chest CT examinations, including initial and follow-up CT studies. We compared the image reports of the initial CT study with the laboratory test results and identified CT patterns suggestive of viral infection.

RESULTS. COVID-19 was misdiagnosed as a common infection at the initial CT study in two inpatients with underlying disease and COVID-19. Viral pneumonia was correctly diagnosed at the initial CT study in the remaining 49 patients with COVID-19 and two patients with adenovirus. These patients were isolated and obtained treatment. Ground-glass opacities (GGOs) and consolidation with or without vascular enlargement, interlobular septal thickening, and air bronchogram sign are common CT features of COVID-19. The “reversed halo” sign and pulmonary nodules with a halo sign are uncommon CT features. The CT findings of COVID-19 overlap with the CT findings of adenovirus infection. There are differences as well as similarities in the CT features of COVID-19 compared with those of the severe acute respiratory syndrome.

CONCLUSION. We found that chest CT had a low rate of missed diagnosis of COVID-19 (3.9%, 2/51) and may be useful as a standard method for the rapid diagnosis of COVID-19 to optimize the management of patients. However, CT is still limited for identifying specific viruses and distinguishing between viruses.

Keywords: coronavirus disease 2019 (COVID-19), CT, infectious diseases, lung disease, SARS-CoV-2

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In December 2019, a large outbreak of a novel coronavirus infection occurred in Wuhan, Hubei Province, China. In humans, coronaviruses are among the spectrum of viruses that cause the common cold as well as more severe respiratory diseases—specifically, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), which have mortality rates of 10% and 37%, respectively [1, 2]; both SARS and MERS are zoonotic infections.

The novel coronavirus that was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses caused a pneumonia outbreak in China [3]. The dis-

ease caused by the virus, named coronavirus disease (COVID-19) by the World Health Organization (WHO), can be spread through human-to-human contact. On January 30, 2020, the WHO declared a global public health emergency against the outbreak of COVID-19. As of February 19, 2020, several cases of COVID-19 had been confirmed in 24 other countries including Thailand, Australia, and the United States. This episode shows the need for rapid and accurate detection and identification methods that can be used in local hospitals and clinics responsible for the diagnosis of COVID-19 and management for patients.

Similarities of clinical features between SARS-CoV-2 infection and previous *Be-*

tacoronavirus infections have been noted. Most patients with previous *Betacoronavirus* infections presented with fever and pneumonia [4]. However, SARS-CoV-2 is distinct from severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Zhu et al. [5] showed that the sequence identity in conserved replicase domains is less than 90% between SARS-CoV-2 and other members of *Betacoronavirus*. Further study is needed to learn more about this difference.

Viral nucleic acid testing is playing an indispensable role in helping to prevent the spread of the COVID-19 epidemic. However, nucleic acid testing has rigorous laboratory specifications and requires a long time before results are available. In addition, some patients with suspected COVID-19 may have initial nucleic acid test results that are false-negative for virus infection, which is harmful for the control of infectious disease. The diagnosis and treatment program (6th version) published by the National Health Commission of the People's Republic of China [6] had defined the diagnosis of viral pneumonia based on radiologic features by radiologists as one of the diagnostic criteria for COVID-19. The accurate diagnosis of viral pneumonia based on chest CT may indicate isolation and plays an important role in the management of patients with suspected SARS-CoV-2 infection, especially when there are no scientifically proven therapies for the treatment of COVID-19. Early discussions suggested that CT should be the preferred modality for diagnosis of COVID-19. However, the use of CT for COVID-19 diagnosis is controversial. In addition, the detailed CT features of COVID-19 have been reported in only a small number of articles in the literature [4, 7, 8].

We retrospectively analyzed the initial and follow-up chest CT images of 51 patients with SARS-CoV-2 infection and two patients with adenovirus infection. To evaluate the misdiagnosis rates of the radiologists, we compared the image reports of initial chest CT studies with the laboratory test results. In addition, we evaluated the initial and follow-up CT studies to identify the CT features of COVID-19 to familiarize radiologists with possible CT patterns of COVID-19 and enable more effective response.

Materials and Methods

Patients

Wuhan authorities suspended all public transport in Wuhan on January 23, 2020, to curb the

TABLE 1: Demographic and Clinical Characteristics of Patients in the Study

Characteristic	All Patients (n = 53)	
	COVID-19 (n = 51)	Adenovirus Infection (n = 2)
Age (y)		
Mean	58	62
Range	26–83	58–66
Sex, no. (%) of patients		
Male	28 (54.9)	1 (50.0)
Female	23 (45.1)	1 (50.0)
Symptoms at presentation, no. (%) of patients		
Fever	46 (90.2)	2 (100)
Fatigue and poor appetite	3 (5.9)	0 (0)
Cough	1 (2.0)	0 (0)
No symptoms	1 (2.0)	0 (0)

Note—Percentages may not add up to 100 because of rounding. COVID-19 = coronavirus disease 2019.

spread of COVID-19. However, as of February 19, 2020, the diagnosis of SARS-CoV-2 has been confirmed in more than 16,000 people in Wuhan.

Our retrospective cohort was composed of 53 patients (29 men and 24 women; age range, 26–83 years; mean age \pm SD, 58 \pm 17 years) with a confirmed positive result for COVID-19 or adenovirus from nucleic acid testing of respiratory secretions, which were obtained by oropharyngeal swab, between January 23, 2020, and January 29, 2020. All virus tests were completed by the laboratory of Tongji Hospital in Wuhan, China. The number of patients in our study group was limited by the fact that there was a shortage of laboratory test kits during the study period. Nucleic acid test results confirmed SARS-CoV-2 in 51 patients, the first 51 cases of COVID-19 diagnosed at our hospital, and adenovirus in two patients.

Of the 51 patients with COVID-19, two patients were in the rehabilitation department: One patient

had been admitted with traumatic brain injury on January 20, and the other patient had undergone surgery for hypertensive cerebral hemorrhage on January 22. Three days after admission, both patients developed fever of unknown origin. Forty-six patients had fever at the time of admission; three, malaise and poor appetite; one, cough; and one, no symptoms (Table 1).

Approval for the retrospective analysis of the patients with SARS-CoV-2 infection and patients with adenovirus was obtained from the Ethics Commission of Tongji Hospital.

CT Technique and Image Interpretation

Two CT scanners (uCT 780, United Imaging; or Somatom Force, Siemens Healthcare) were used for all chest CT examinations. Conventional CT was performed with the patient in the supine position during end-inspiration. Technologists who

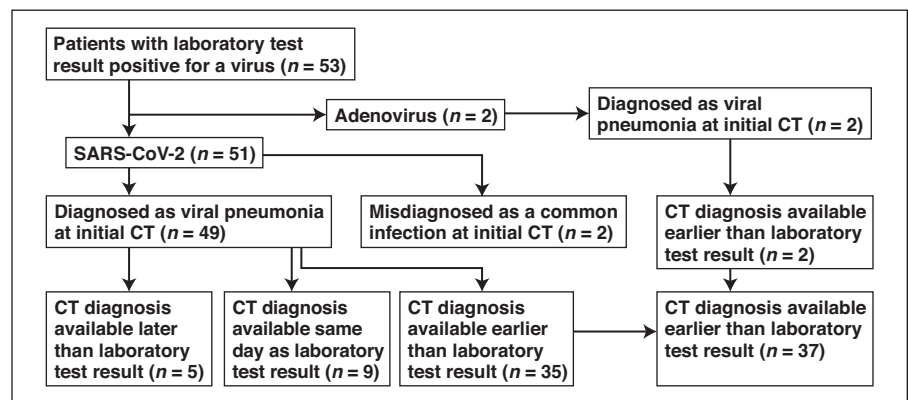


Fig. 1—Flowchart shows time difference between positive laboratory test results and positive CT findings for coronavirus disease (COVID-19) and adenovirus infection in our study group of 53 patients. SARS-CoV-2 = severe acute respiratory syndrome

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performed CT of patients with suspected COVID-19 were required to wear protective garments.

Because the study is a retrospective analysis, no standard CT protocol was applied. All CT images were reconstructed to 1.25-mm thin slices. Multiplanar images were obtained using the multiplanar reformatting (MPR) technique on a workstation.

Every chest CT examination was read first by one radiologist and was then checked by another radiologist; the radiologists had 7–20 years' experience in interpreting chest CT. In patients with CT findings suggestive of viral pneumonia, the radiologists informed the clinician immediately. The clinician would then order immediate isolation of the patient for clinical monitoring and treatment.

CT Review

We reviewed all chest CT examinations and corresponding image reports of patients in the cohort. We compared the time of the laboratory test result confirming a positive diagnosis of a virus and the time of the chest CT report confirming a positive diagnosis of viral pneumonia.

Patients with a diagnosis of viral pneumonia made by radiologists were defined as true-positive cases, and patients with a diagnosis of a common infection made by radiologists were defined as false-negative cases. We calculated the rate of misdiagnosis and estimated the performance of radiologists based on chest CT to help in the management of patients. We sought to identify the CT features of lesions suggestive of COVID-19 based on the initial CT images and identify the radiographic findings suggestive of COVID-19 transformation on follow-up CT images. We tried to determine whether there are CT features that can be used to differentiate SARS-CoV-2 infection from infections caused by other viruses.

Results

In our retrospective cohort of 53 patients, a total of 99 chest CT examinations had been performed as of February 9. The mean number of CT examinations per patient is 1.9 (99/53). Viral pneumonia was diagnosed in 51 of the 53 (96.2%) patients; these 51 patients include 49 patients with confirmed SARS-CoV-2 infection and two patients with confirmed adenovirus infection. The misdiagnosis rate of viral infec-

tion was 3.8% (2/53). CT findings were positive for viral infection before laboratory results were positive for viral infection in 37 of 53 (69.8%) patients (Fig. 1). The mean lead time in diagnosis of viral infection yielded by CT compared with laboratory results was 3.0 days.

In the next sections, we discuss the CT features of 51 patients with confirmed SARS-CoV-2 infection and of two patients with confirmed adenovirus infection.

TABLE 2: Initial CT Findings of 51 Patients With Coronavirus Disease (COVID-19)

CT Findings	No. (%) of Patients
GGOs and consolidation	
Absence of both GGOs and consolidation	2 (3.9)
Presence of GGOs with consolidation	28 (54.9)
Presence of GGOs without consolidation	18 (35.3)
Presence of consolidation without GGOs	3 (5.9)
Vascular enlargement	42 (82.4)
Interlobular septal thickening in a crazy-paving pattern	36 (70.6)
Air bronchogram sign	35 (68.6)
Air trapping	6 (11.8)
"Reversed halo" sign	2 (3.9)
Discrete pulmonary nodules	
Nodules with halo sign	9 (17.6)
Nodules without halo sign	2 (3.9)
Bronchus deformation due to fibrosis and striplike lesions	10 (19.6)
Pleural effusion	1 (2.0)
Mediastinal lymphadenopathy	0 (0)

Note—GGOs = ground-glass opacities.



Fig. 2—77-year-old woman with coronavirus disease (COVID-19). Transverse CT scan shows multiple ground-glass opacities and consolidation with thickened intralobular and interlobular septum (*white arrow*). Air bronchogram sign (*arrowhead*) and air trapping (*black arrow*) are present.

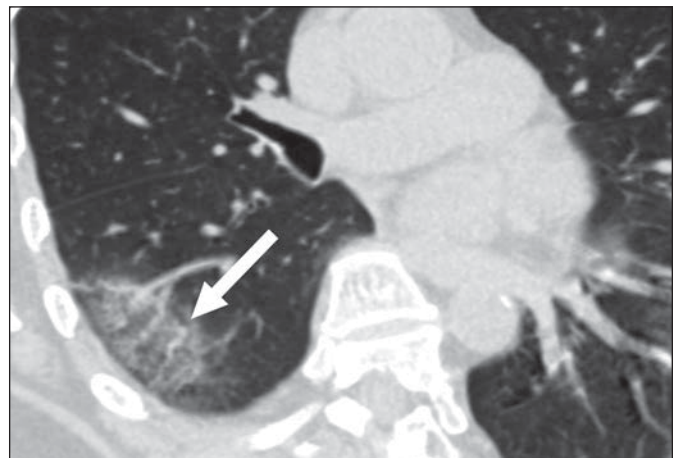


Fig. 3—61-year-old woman with coronavirus disease (COVID-19). Oblique transverse CT image shows ground-glass opacities with vascular enlargement (*arrow*).

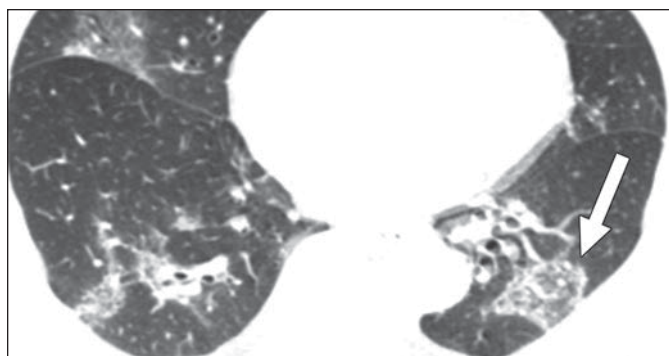


Fig. 4—68-year-old man with coronavirus disease (COVID-19). Transverse CT scan shows “reversed halo” sign in left lower lobe (arrow).

CT Features of Coronavirus Disease

Initial CT scans—The initial chest CT studies of the 51 patients with COVID-19 showed that disease affected all five lobes in 38 (74.5%) patients, both lower lobes in eight (15.7%) patients, the right lower lobe in three patients (5.9%), the left upper lobe and right lower lobe in one patient (2.0%), and the left upper lobe and right middle lobe in one patient (2.0%). The lesions were predominantly peripheral and subpleural in 49 (96.1%) patients, and there were fewer lesions along the bronchovascular bundles.

GGO and consolidation are two main signs of COVID-19 lesions on CT images. CT showed singular or multiple irregular areas of GGO or consolidation or both in 49 of the 51 (96.1%) patients. In the remaining two (3.9%) patients, neither GGO nor consolidation was seen on CT (Table 2).

We noted additional signs of COVID-19 lesions on CT images. CT showed ill-defined GGO or consolidation (Fig. 2) with vascular enlargement in 42 (82.4%) patients (Fig. 3), interlobular septal thickening appearing in a crazy-paving pattern in 36 (70.6%) patients,

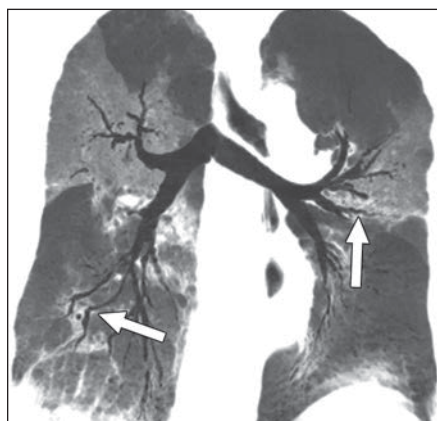


Fig. 5—66-year-old man with coronavirus disease (COVID-19). Minimum-intensity-projection CT image shows bronchus deformation due to fibrosis and striplike lesions (arrows).

the air bronchogram sign in 35 (68.6%) patients, air trapping in six (11.8%) patients (Fig. 2), and “reversed halo” sign in two (3.9%) patients (Fig. 4).

CT showed that 11 (21.6%) patients had discrete pulmonary nodules: Nine patients had nodules with a halo sign and two had solid nodules without a halo sign. Ten (19.6%) patients had bronchus deformation due to fibrosis and striplike lesions (Fig. 5). One (2.0%) patient showed pleural effusion. No patients had mediastinal lymphadenopathy.

Follow-up CT scans—As of February 19, 24 patients with an initial chest CT examination showing lesions suggestive of a viral infection had undergone follow-up CT, one of whom had five follow-up CT examinations. The mean time between the initial and follow-up CT studies was 5.0 days (range, 2–15 days).

For the patient with five follow-up CT examinations, CT showed increasing density of consolidation on the first and second follow-up studies, which indicates marked disease progression, and showed findings suggestive of improvement on the third and fourth follow-up studies; however, the increasing number of GGOs detected on the fifth follow-up CT study suggested mild disease progression (Fig. 6).

Follow-up CT showed mild or marked disease progression in 18 of 24 (75.0%) patients. As the disease advances, the upper lobes are affected, even all five lobes of both lungs in some patients. In five patients, follow-up CT showed improvement with the appearance of fibrosis and resolution of GGOs.

Misdiagnosis of coronavirus disease—COVID-19 was misdiagnosed as a common infection in two patients on the basis of CT findings. The patients were inpatients in the rehabilitation department. CT of one patient showed opacities and consolidations along the bronchovascular bundles and unilateral pleural effusion. CT of the other patient showed dense consolidation in the subpleural area without GGO.

CT Findings of Adenovirus Infection

CT of one of the two patients with confirmed adenovirus infection showed ill-defined patchy GGOs, segmental and subpleural consolidations in both lungs, and pleural effusion. CT of the other patient showed subpleural GGOs and consolidation with vascular enlargement, interlobular septal thickening, and air bronchogram sign. The CT findings seen in these two adenovirus cases (Fig. 7) are similar to the CT findings seen in the COVID-19 cases.

Discussion

In our study, viral pneumonia was diagnosed on the basis of CT findings in 49 of 51 (96.1%) patients with COVID-19; the remaining two patients with COVID-19 were bedridden inpatients with underlying diseases. The clinician prescribed isolation and supportive treatment in time for recovery in these 49 patients. Of the 53 patients in our study group, positive CT findings diagnostic of viral pneumonia were available before a positive laboratory test result in 37 (69.8%) patients. The diagnosis of viral pneumonia based on CT was available 3.0 days earlier than that based on nucleic acid test results. Although when in terms of disease progression a clinician chooses to order nucleic acid testing may affect the accuracy of the test results, we are confident that CT has a high accuracy and may be useful as a standard method for the diagnosis of COVID-19. The use of CT for the diagnosis of viral pneumonia allows patients with suspected SARS-CoV-2 infection to be isolated and treated in time for recovery, thus optimizing patient management.

The CT patterns of viral pneumonia are related to the pathogenesis of the viral infection. Viruses of the same family (e.g., Coronaviridae) have a similar pathogenesis [9]. Therefore, viral pneumonia caused by different viruses from the same virus family exhibit a similar pattern on chest CT images. SARS-CoV-2 belongs to the genus *Betacoronavirus* according to genome analysis [10]. SARS-CoV and MERS-CoV were identified as members of the family Coronaviridae in 2003 and 2012, respectively. Some CT features of patients with confirmed COVID-19 that were frequently seen in patients in our investigation are similar to the CT features of SARS and MERS. Of the 51 patients in our COVID-19 cohort, only two (3.9%) did not have GGO or consolidation. Therefore, our results show that GGO and consolidation were two main signs on CT images of COVID-19 lesions.

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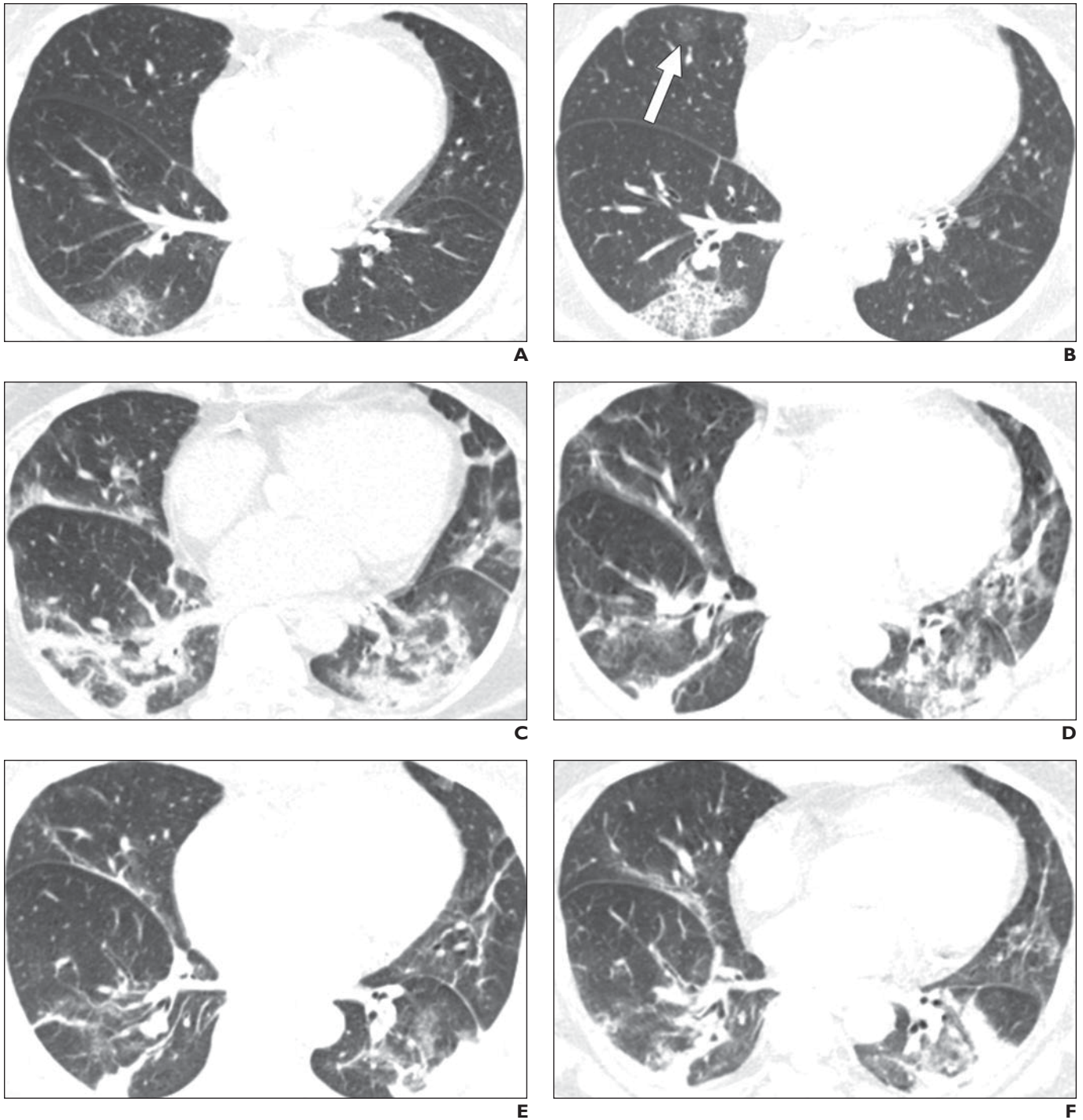


Fig. 6—61-year-old woman with coronavirus disease (COVID-19) diagnosed on January 27, 2020. She presented with fever and cough and underwent five follow-up CT examinations after initial chest CT.

A, Initial transverse CT image obtained on January 16 shows patchy ground-glass opacities (GGOs) and consolidation in right lower lobe.

B, Transverse CT image obtained on January 19 shows subtle GGO in right middle lobe (*arrow*) that was not present on initial scan (**A**) and reveals that consolidation in right lower lobe is larger than on initial scan.

C, Transverse CT image obtained on January 24 shows multiple patchy GGOs and consolidations are present in both lungs with reticular pattern.

D, Transverse CT image obtained on January 27 shows residual consolidation and fibrosis.

E, Transverse CT image obtained on January 31 shows some consolidations have resolved.

F, Transverse CT image obtained on February 4 shows increased consolidation.

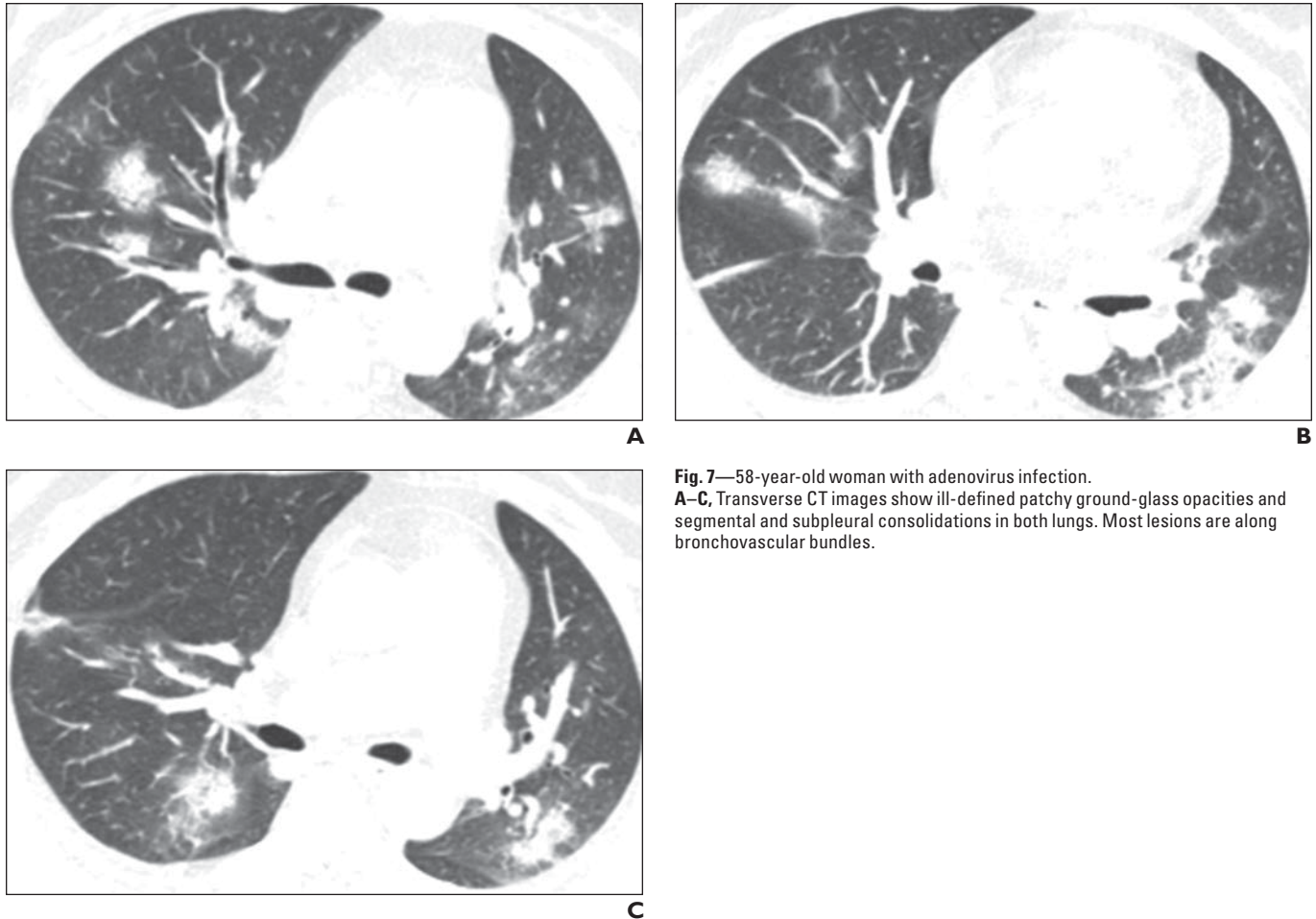


Fig. 7—58-year-old woman with adenovirus infection. **A–C**, Transverse CT images show ill-defined patchy ground-glass opacities and segmental and subpleural consolidations in both lungs. Most lesions are along bronchovascular bundles.

Angiotensin-converting enzyme II is a key molecule involved in the development and progression of acute lung failure [11]. SARS-CoV induces direct lung injury by involving angiotensin-converting enzyme, which contributes to diffuse alveolar damage [9]. This may explain the pathologic mechanism of GGO and consolidation as well as the rapid changes in CT findings. Our results support the observed trend that bilateral GGOs or consolidations on chest imaging should prompt the radiologist to suggest COVID-19 as a possible diagnosis [12]. However, we observed that some patients had difficulty breathing during CT, so obtaining perfect CT images during end-inspiration may be difficult in this population. Therefore, when reviewing CT examinations, radiologists should pay attention to differentiating GGO or consolidation from motion artifact. Furthermore, we found that all the CT features seen on the initial chest CT examinations of patients with COVID-19—GGO, consolidation, vascular enlargement, interlobular sep-

tal thickening, air bronchogram sign, and air trapping—are similar to the CT features of SARS and MERS. These CT features are caused by alveolar and interstitial pulmonary injury and edema.

We also observed some CT features of COVID-19 that differ from the CT features of SARS and MERS. In our study group of patients with COVID-19, CT showed a reversed halo sign in two (3.9%) patients and pulmonary nodules with a halo sign in nine (17.6%) patients. These findings are not mentioned, to our knowledge, in the studies in the literature about SARS and MERS. In addition, unifocal involvement is more common than multifocal involvement on chest CT of patients with SARS and patients with MERS [13, 14]. However, the opposite is seen on chest CT of patients with COVID-19: Multifocal involvement was more common than unifocal involvement in our study. This finding is supported by the study of Chung et al. [8].

As the severe infectious diseases of SARS or MERS progress, lung parenchymal ab-

normalities eventually spread to the central area and bilateral upper lobes [13, 14]. In our study, COVID-19 progression on CT images supported this CT pattern of progression. In our cohort of patients with COVID-19, the distribution of disease was predominantly peripheral (subpleural) and confined to the middle and lower zones of the lung on the initial chest CT. Follow-up CT showed that, as the disease advanced, consolidation and coalescing infiltrates pervaded the lungs and the upper lobes were affected; in fact, in some patients, all five lobes of both lungs were affected, with CT showing white lungs. In our study group, the increasing numbers of GGOs and densities of consolidation indicated disease progression, whereas the appearance of fibrosis and resolution of GGO or consolidation indicated improvement. Deformation of the bronchus due to fibrosis and striplike lesions may cause irreversible injury and may affect the respiratory function of the patient. We noted that the initial CT images showed fibrosis and striplike lesions with de-

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formation of the bronchus in 10 (19.6%) patients: These cases indicate that COVID-19 lesions may be present before symptoms develop and became obvious to patients and that CT should have been performed earlier in these cases.

Of the patients who underwent follow-up CT, CT showed progression in 75.0% (18/24). One patient who underwent five follow-up CT examinations was in an unstable condition and showed mild progression on the fifth follow-up study after initial marked progression on the first and second follow-up studies and improvement on the third and fourth follow-up studies. Although WHO's preliminary estimate shows COVID-19 has a relatively lower mortality rate compared with the mortality rates of SARS and MERS, our study showed that most patients with COVID-19 may experience progression. However, we did not compare the CT findings with the symptoms of the patients. Further study might be needed.

We found that two patients with COVID-19 did not present with CT patterns typical of viral pneumonia. Because these two patients did not have CT features and distribution typical of COVID-19, radiologists could not differentiate COVID-19 from a common bacterial infection or coinfection with bacterial infection. These misdiagnosed cases indicate that we should consider COVID-19 in the differential diagnosis when inpatients show fever of unknown origin.

Adenoviruses belong to the Adenoviridae family, a family of double-stranded DNA viruses. Some studies in the literature have reported that adenovirus pneumonia shows bilateral multifocal GGOs with lobar or segmental distribution indicative of bronchopneumonia, which resembles bacterial pneumonia [11, 15]. One of the two patients in our study with confirmed adenovirus infection had these CT findings. The other patient had CT findings showing GGO and consolidation similar to the CT findings of COVID-19.

In this retrospective cohort of COVID-19 cases and adenovirus cases confirmed between January 23, 2020, and January 29, 2020, no children were included. The lack of children with COVID-19 in our study group is consistent with a description in a study in the literature; the authors of that study [16] suggested that children might be less likely to become infected with SARS-CoV-2 than

adults or, if infected, may show milder symptoms than adults. This potential characteristic of SARS-CoV-2 seen in our study group is similar to MERS-CoV: One characteristic feature of MERS-CoV is the extremely low number of children who were affected by the disease, and the course of pediatric MERS cases is usually mild or asymptomatic [17]. However, we continue to collect information on children's infections that can be new sources of infection. Whether the chest CT features of children with COVID-19 are similar to those of adults with COVID-19 needs further study.

In conclusion, our study showed that CT had a low rate of missed diagnosis of COVID-19 (3.9%, 2/51) and thus may be useful as a standard method for the diagnosis of COVID-19 based on CT features and rules of transformation. Rapid diagnosis can lead to early control of potential transmission. With CT diagnosis of viral pneumonia, patients with suspected disease can be isolated and treated in time so that the management of patients will be optimized, especially for the hospitals or communities lacking nucleic acid testing kits. However, for the identification of specific viruses, CT is still limited. It is valuable for radiologists to recognize that the CT findings of COVID-19 overlap with the CT findings of diseases caused by viruses from a different family, such as adenovirus, and have differences as well as similarities with viruses within the same family, such as SARS-CoV and MERS-CoV.

Acknowledgments

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