Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHEST

A 53-Year-Old Man Presents to the ED With Shortness of Breath, Cough, and Fever

Leonid Roshkovan, MD; Jeffrey C. Thompson, MD; Neil Chatterjee, MD; Maya Galperin-Aizenberg, MD; and Sharyn I. Katz, MD

CASE PRESENTATION: A 53-year-old man presented to the ED at a time of low severe acute respiratory syndrome coronavirus 2, also known as coronavirus disease 2019 (COVID-19), prevalence and reported 2 weeks of progressive shortness of breath, dry cough, headache, myalgias, diarrhea, and recurrent low-grade fevers to 39°C for 1 week with several days of recorded peripheral capillary oxygen saturation of 80% to 90% (room air) on home pulse oximeter. Five days earlier, he had visited an urgent care center where a routine respiratory viral panel was reportedly negative. A COVID-19 reverse transcriptase polymerase chain reaction test result was pending at the time of ED visit. He reported a past medical history of gastroesophageal reflux disease that was treated with famotidine. Travel history included an out-of-state trip 3 weeks earlier, but no recent international travel.

CHEST 2021; 159(2):e107-e113

Physical Examination Findings

His temperature was 39°C; his heart rate was 82 beats per minute; his BP was 123/75 mm Hg; his respiratory rate was 18 breaths/min, and his oxygen saturation level was 96% (room air). The patient appeared acutely ill. Faint crackles were appreciated at the lung bases with associated rhonchi. The cardiovascular examination was normal. There was no jugular venous distension or lower extremity edema. The remainder of the physical examination was unremarkable.

Diagnostic Studies

The results of a basic metabolic panel and liver function tests were normal. A CBC count revealed a WBC count of 3.2 × 10^3/μL (normal, 4.0-11.0 × 10^3/μL) with mild lymphopenia of 16.4% (normal, 20%-47%), normal hemoglobin and hematocrit levels, and a slightly depressed platelet count of 113 × 10^3/μL (normal, 150-400 × 10^3/μL). Respiratory viral panel results were negative for influenza A, influenza B, parainfluenza (1-4), adenovirus and respiratory syncytial virus A and B, rhinovirus, adenovirus, *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, and human metapneumovirus.

Chest radiographs that had been obtained at the urgent care facility were normal (Fig 1A, B). Given worsening symptoms and reported hypoxia at home, a chest CT image was obtained that revealed multifocal patchy ground-glass opacities in a peripheral distribution (Fig 2A,B) that was also seen on follow-up chest radiography (Fig 1C).

AFFILIATIONS: From the Department of Radiology (L. Roshkovan, N. Chatterjee, M. Galperin-Aizenberg, and S. I. Katz) and the Division of Pulmonary, Allergy, and Critical Care (J. C. Thompson), University of Pennsylvania Perelman School of Medicine, Philadelphia, PA.

CORRESPONDENCE TO: Leonid Roshkovan, MD; e-mail: leonid.roshkovan@pennmedicine.upenn.edu

DOI: https://doi.org/10.1016/j.chest.2020.09.243

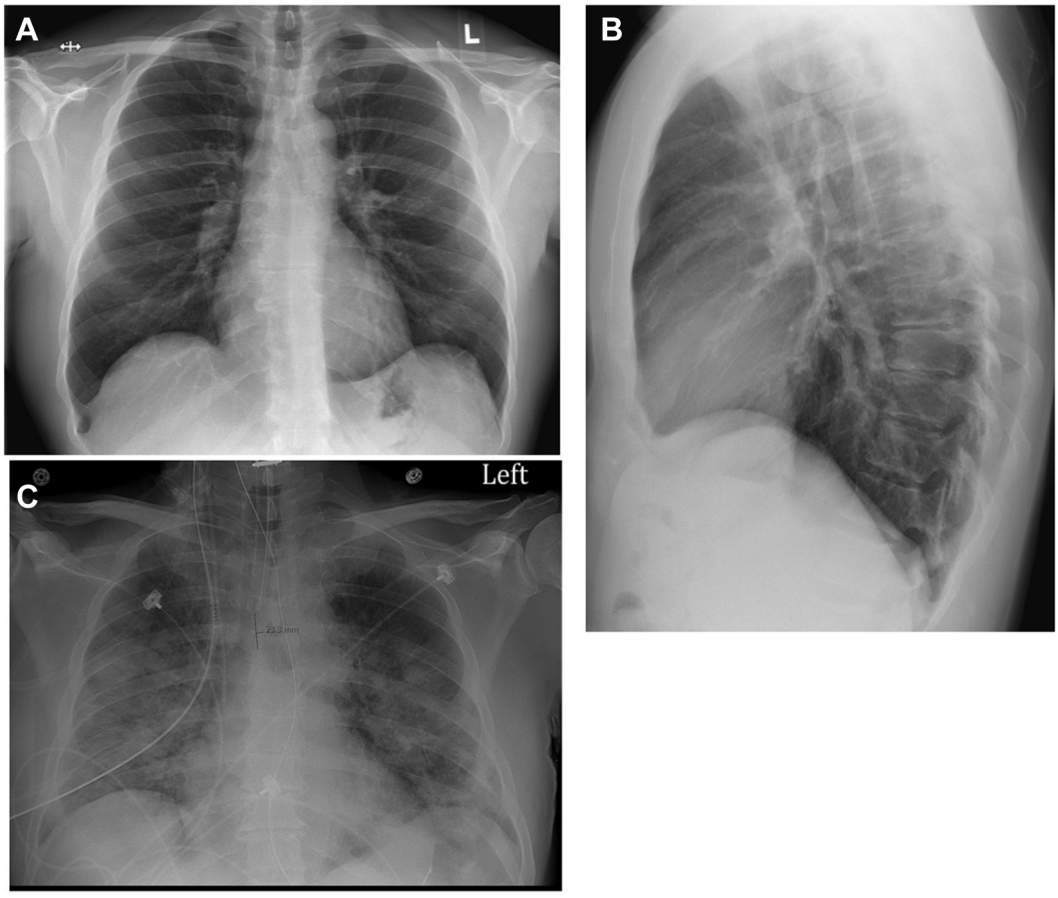

Figure 1 – *A-C, Chest radiographs at presentation and follow up. A and B, A posteroanterior and lateral view of the chest was obtained after 1 week of symptoms at an outpatient clinic and revealed no evidence of an acute process in the chest. C, Seven days later, a follow-up portable anteroposterior chest radiograph that was performed for worsening symptoms demonstrates multifocal airspace opacities that are consistent with pneumonia.*

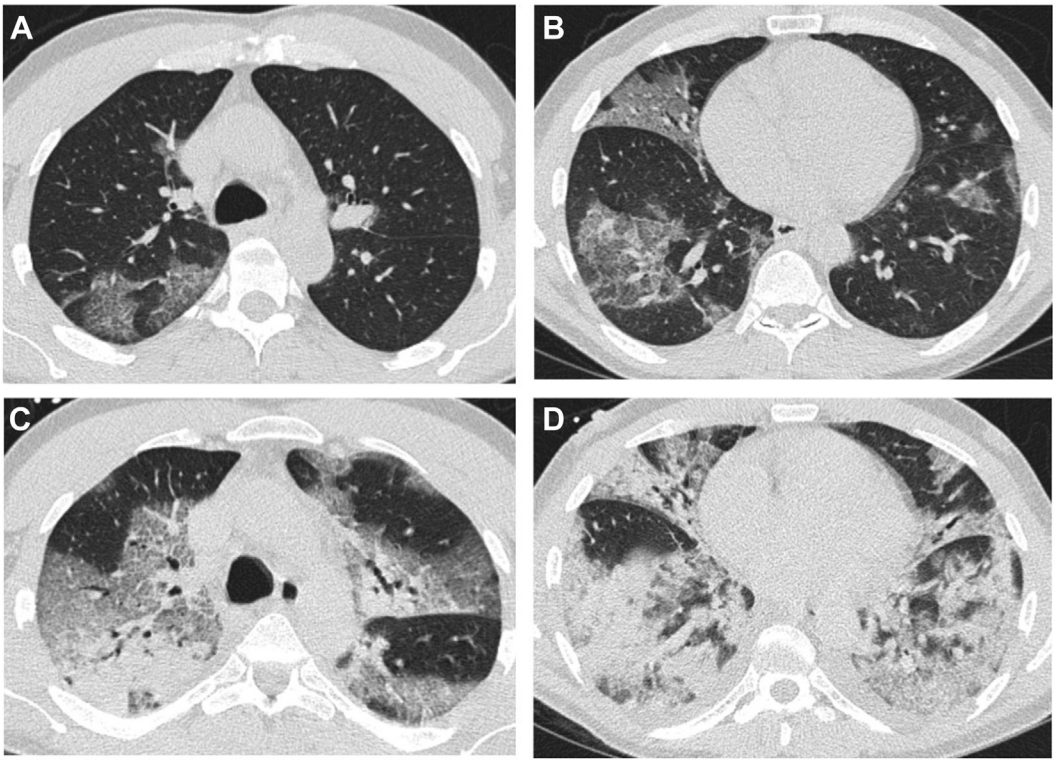

Figure 2 – *A-D, CT chest image at presentation and follow up. A and B, CT examination performed at presentation to the ED, 12 days after the start of symptoms, reveals bilateral patchy, slightly nodular ground-glass opacities in a peripheral and basilar distribution. C and D, Follow-up CT performed 8 days later reveals marked worsening of the pulmonary opacities that now are largely consolidated.*

What is the diagnosis?

Answer: The patient was diagnosed with severe acute respiratory syndrome coronavirus 2, also known as coronavirus disease 2019

Discussion

The initial presenting features of severe acute respiratory syndrome coronavirus 2 infection, also known as coronavirus disease 2019 (COVID-19), can be nonspecific; however, several factors may lead the clinician to suspect COVID-19 infection. First, in regions where the prevalence of the disease is low, alternative diagnoses such as viral, bacterial, organizing, or eosinophilic pneumonias should be considered; however, in areas where COVID-19 is more prevalent, the likelihood of this diagnosis increases. The rapid progression of shortness of breath and hypoxia, leukopenia, and lymphopenia, particularly when accompanied by fever and cough, myalgias, and less commonly diarrhea, in an otherwise healthy patient suggests COVID-19. Negative respiratory viral panels that exclude influenza and a recent history of travel to areas of high prevalence of COVID-19 should further raise suspicion of this disease entity, even in the setting of low local prevalence.

The diagnosis is established typically with a RT-PCR test taken from nasal swab sample. The sensitivity of RT-PCR for the detection of active COVID-19 has been reported to be in the range of 38% to 88% and depends on several factors that include site of sample acquisition and kit manufacturer. Repeat testing usually is performed if there is a moderate or high clinical suspicion for COVID-19 infection in the setting of a first negative result, because initially negative RT-PCR may take up to 4 days to convert to positive.

The current international recommendations by the Fleischner Society (Table 1) for imaging use in patients with suspected COVID-19 do not recommend imaging in the setting of positive RT-PCR and mild symptoms (absence of significant pulmonary dysfunction) with a low risk for advancement to severe disease. Imaging is indicated in patients with mild clinical features and risk factors for disease progression (eg, age >65 years, diabetes mellitus, and renal or cardiovascular disease) or patients with moderate-to-severe disease, regardless of RT-PCR results. Additionally imaging is recommended when alternative diagnosis is sought or in patients with known COVID-19 who present with worsening respiratory status. Chest radiographs are more readily available and present less risk to health-care providers when obtained portably, but they are less sensitive for detection of mild disease compared with CT images. The positive and negative predictive value of chest radiography for active COVID-19 infection has been estimated at 61% to 77% and 73% to 78%, respectively, with a sensitivity of approximately 69% to 75%, which has led to an interest in artificial intelligence software for enhanced detection. When present, the findings of COVID-19 on chest radiography include subtle pulmonary opacities, with or without consolidations, more commonly bilateral, peripheral, and lower lobe predominant. Interstitial findings have also been reported on chest radiography presenting with both reticular and reticulonodular imaging patterns. The extent of lung opacities on chest radiography has been shown to correlate with the severity of disease and likelihood of the development of associated pulmonary complications. Although not specific, the presence of pulmonary opacities on chest radiography in patients who clinically are suspected of COVID-19 increases the pre-test probability of disease when RT-PCR test results are not available.

The sensitivity of CT imaging for COVID-19 has been reported to be between 70% and 97%, possibly

TABLE 1] Summary of Fleischner Society Recommendations for Imaging in the Setting of the COVID-19 Pandemic

• Imaging is not indicated routinely as a screening test for COVID-19 in asymptomatic individuals.
• Imaging is not indicated for patients with mild features of COVID-19, unless they are at risk for disease progression.
• Imaging is indicated for patients with moderate-to-severe features of COVID-19, regardless of COVID-19 test results.
• Imaging is indicated for patients with COVID-19 and evidence of worsening respiratory status.
• In a resource-constrained environment in which access to CT imaging is limited, chest radiography may be preferred for patients with COVID-19, unless features of respiratory worsening warrant the use of CT imaging.
• Daily chest radiographs are not indicated in stable intubated patients with COVID-19.
• CT imaging is indicated in patients with functional impairment and/or hypoxemia after recovery from COVID-19.
• COVID-19 testing is indicated in patients incidentally found to have findings suggestive of COVID-19 on a CT scan.

Data from Rubin et al. COVID-19 = coronavirus disease 2019.

TABLE 2] Summary of the Radiologic Society of North America CT Imaging Reporting Guidelines in the Setting of People Suspected of COVID-19 Infection

Reporting Classification	CT Findings	Clinical Implications
Typical appearance	Peripheral, bilateral ground-glass opacities	Common findings of COVID-19 are present.
	Multifocal rounded ground-glass opacities	Other diseases can have a similar appearance (ie, other viral pneumonia, organizing pneumonia).
	Ground-glass opacities with/without consolidation or intralobular septal thickening	…
	Reverse halo sign (atoll sign)	…
Indeterminate appearance	Ground-glass opacities with unilateral, diffuse, perihilar or no specific distribution	Imaging findings can be seen with COVID-19 but are also present in a variety of infectious and noninfectious inflammatory processes.
	Few ground-glass opacities	…
Atypical appearance	Lobar or segmental consolidation without ground-glass opacity	…
	Small discrete nodules	…
	Lung cavitation	…
	Interlobular septal thickening with pleural effusions	Imaging features are uncommon for COVID-19 pneumonia; consider alternate diagnosis.
Negative for pneumonia	Clear lungs	No evidence of COVID-19 is present.

Data from Simpson et al. See Table 1 legend for expansion of abbreviation.

outperforming RT-PCR in the detection of early COVID-19 pneumonia. However, some have reported that up to 18% of patients with active COVID-19 have no radiographic or CT chest findings, especially early in the disease. As a result, CT scans of the chest are not recommended for routine screening or to exclude active COVID-19 pneumonia. There has been a large degree of variability in the reported specificity of CT scanning for COVID-19 pneumonia, with reported values that range from 7% to 100%. Reports of low specificity of CT scans are attributable, in part, to overlap in the imaging features of COVID-19 pneumonia with a number of other disease entities that include organizing pneumonia, either cryptogenic or due to other disease entities such as drug toxicity, acute eosinophilic pneumonia, and other viral pneumonias. Therefore, in areas of low prevalence of COVID-19, alternative diagnoses may be considered even in the presence of CT features that are typical of COVID-19 pneumonia.

On CT imaging, the presence of peripheral bilateral lower lobe predominant ground-glass opacities, with or without consolidations, is considered typical for COVID-19 pneumonia in the appropriate clinical setting; the presence of this pattern can increase confidence of the diagnosis of COVID-19 (Fig 2, A and B). Pleural effusions or thoracic lymphadenopathy are uncommon in the setting of COVID-19.

Recently, the Radiologic Society of North America published a consensus statement for describing CT imaging findings for patients who are suspected of COVID-19 pneumonia (Table 2). Four categories for reporting CT findings in COVID-19 pneumonia include typical, intermediate, atypical, and negative. The purpose of these guidelines is to provide familiarity with the CT findings that are commonly and uncommonly observed in COVID-19 pneumonia and also to provide guidance to the medical community for use of CT report findings in the setting of suspected COVID-19 pneumonia. The positive and negative predictive values of these Radiologic Society of North America criteria for COVID-19 are still to be determined; however, this reporting system is currently being widely adopted in patients suspected of COVID-19 infection. Similar COVID-19 CT reporting criteria have been proposed by other international societies and are, likewise, yet to be fully validated.

For example, the Dutch COVID-19 Reporting and Data System (RADS) uses a five-category assessment scheme of pulmonary CT findings and their correlating

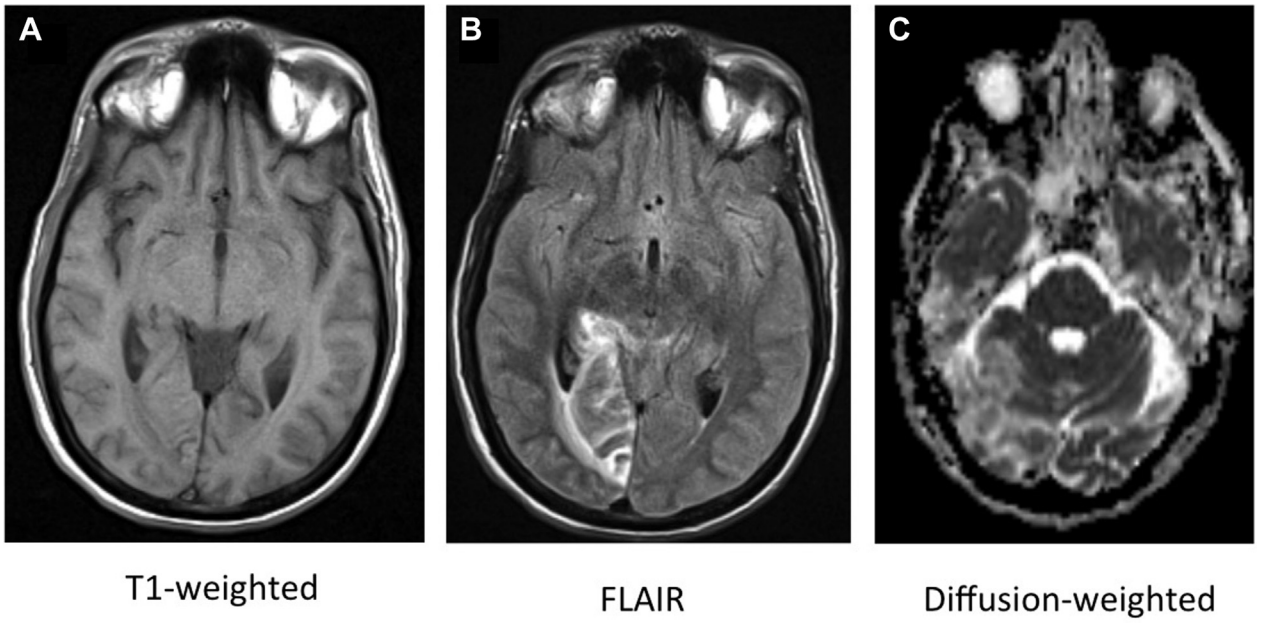

Figure 3 – *A-C, Acute right posterior inferior cerebellar artery stroke. At day 29 of his inpatient stay, the patient presented with altered mental status and was diagnosed with an acute ischemic stroke that involved the right posterior inferior cerebellar artery distribution. A, Axial T1-weighted imaging shows no evidence of hemorrhage. B, Axial fluid-attenuated inversion recovery reveals high signal on this T2-weighted sequence in keeping with edema in the right cerebellum. C, Diffusion-weighted imaging shows restricted diffusion in the region of the right cerebellum. FLAIR = fluid-attenuated inversion recovery.*

suspicion level for pulmonary involvement by COVID-19. A CO-RADS category 5 implies a very high level of suspicion for pulmonary involvement by COVID-19, based on typical CT findings. CT findings were considered typical when there were ground-glass opacities with or without consolidations in lung regions close to visceral pleural surfaces, including the fissures, and a multifocal bilateral distribution. By comparison, a CO-RADS 1 implies a very low level of suspicion with normal CT results or CT findings of unequivocal noninfectious origin. This scoring system has a reported area under the curve of 0.91 by the authors for the prediction of a positive RT-PCR result.

Clinical Course

The patient was subsequently confirmed to be positive for infection with COVID-19 by RT-PCR. This patient experienced worsening hypoxemia and was maintained on supplemental oxygen through high-flow nasal cannula. Hydroxychloroquine and a 5-day course of azithromycin were also given. A CT chest scan that was obtained 8 days after admission (Fig 2, C and D) revealed marked worsening of the previously seen pulmonary opacities that now were more extensive and consolidative and showed evidence of evolving changes of diffuse alveolar damage. On the way back to his room from the CT scanner, the patient experienced respiratory failure and was intubated and transferred to the ICU. Hospitalization was complicated by methicillin-sensitive *Staphylococcus aureus* bacteremia and presumed methicillin-sensitive *Staphylococcus aureus* pneumonia 3 days after intubation that contributed to the severity of his ARDS and prolonged intubation, which was treated with cefazolin. Tracheostomy was performed 22 days after intubation. The patient also experienced a cerebral vascular accident in the right posterior inferior cerebellar artery diagnosed at day 29 of his hospital stay (Fig 3), presumably due to the hypercoagulable state induced by COVID-19. COVID-19 has been reported to be associated with an increased risk of cerebrovascular events and pulmonary and systemic arterial emboli in this patient population. After three consecutive RT-PCR tests that showed no evidence of active shedding of COVID-19, the patient was discharged to a rehabilitation facility for recovery after 38 days in the hospital.

Clinical Pearls

1. *A negative CT chest scan result does not exclude COVID-19 pneumonia.*
2. *CT imaging appears to be more sensitive for the detection of COVID-19 pneumonia (ranging from 70%-97%) than chest radiography (ranging from*

69%-75%) and RT-PCR (ranging from 38%-88%).Typical findings on CT imaging include peripheral bilateral lower lobe predominant ground-glass opacities.

3. *Imaging should be reserved for patients with mild symptoms and clinical risk factors, patients with moderate-to-severe symptoms, those with worsening respiratory status, or cases for which an alternative diagnosis is suspected.*

Acknowledgments

Financial/nonfinancial disclosures: None declared.

Other contributions: *CHEST* worked with the authors to ensure that the Journal policies on patient consent to report information were met.

Suggested Readings

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.

Dennie C, Hague C, Lim RS, et al. Canadian Association of Thoracic Radiology/Canadian Association of Radiologists consensus statement regarding chest imaging in suspected and confirmed COVID-19. *Can Assoc Radiol J*. 2020;71(4):470-481.

Litmanovich DE, Chung M, Kirkbride RR, Kicska G, Kanne JP. Review of chest radiograph findings of COVID-19 pneumonia and suggested reporting language [published online ahead of print June 9, 2020]. J Thorac Imaging. https://doi.org/10.1097/RTI.0000000000000541.

Murphy K, Smits H, Knoops AJG, et al. COVID-19 on the chest radiographs: a multireader evaluation of an artificial intelligence system. *Radiology*. 2020;296(3):E166-E172.

Prokop M, van Everdingen W, van Rees Vellinga T, et al. CO-RADS: a categorical CT assessment scheme for patients with suspected COVID-19: definition and evaluation. *Radiology*. 2020;296(2):E97-E104.

Rodriguez-Pardo J, Fuentes B, Alonso de Lecinana M, et al. Acute stroke care during the COVID-19 pandemic: Ictus Madrid Program recommendations [in Spanish]. *Neurologia*. 2020;35(4):258-263.

Rubin GD, Ryerson CJ, Haramati LB, et al. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. *Chest*. 2020;158(1):106-116.

Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19) imaging reporting and data system (COVID-RADS) and common lexicon: a proposal based on the imaging data of 37 studies. *Eur Radiol*. 2020;30(9):4930-4942.

Simpson S, Kay FU, Abbara S, et al. Radiological Society of North America Expert Consensus Statement on reporting chest CT findings related to COVID-19. Endorsed by the Society of Thoracic Radiology, the American College of Radiology, and RSNA. *J Thorac Imaging*. 2020;35(4):219-227.

Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. *Eur Radiol*. 2020;30(8):4381-4389.