



# Extensive Nonsegmental Pulmonary Perfusion Defects on SPECT/CT as an Early Sign of COVID-19 Infection

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## Abstract

### Keywords

- ▶ pulmonary embolism
- ▶ perfusion imaging
- ▶ SPECT/CT
- ▶ COVID-19
- ▶ inflammation
- ▶ pneumonia

We describe a hospitalized patient with confirmed coronavirus disease 2019 in whom the initial chest computed tomography (CT) was negative, while subsequent perfusion single-photon emission computed tomography/computed tomography imaging revealed extensive nonsegmental perfusion defects in addition to newly developing parenchymal densities. Possible reasons for these findings and their relationship to the multisystem severe acute respiratory syndrome coronavirus 2 infection are discussed in this article.

## Introduction

Coronavirus disease 2019 (COVID-19) is a highly contagious infectious disease caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). In the symptomatic patient, it is predominantly an acute respiratory disease accompanied by fever, shortness of breath, and cough, among other symptoms. The ongoing global pandemic has to date infected over 16.5 million people, resulting in approximately 655,000 deaths worldwide.<sup>1</sup>

Consequential lung inflammation, resulting in COVID-19 associated pneumonia, is usually diagnosed by characteristic changes on chest X-ray or thoracic computed tomography (CT) imaging. Typically, chest CT demonstrates nonspecific

bilateral abnormalities, with ground glass opacities in milder forms progressing to widespread consolidation in more severe forms of disease.<sup>2–5</sup> Eventually, progressive atypical respiratory system distress may develop over time, and other organ systems are frequently affected including the central nervous system, heart, and kidneys. This may be related to the propensity of SARS-CoV-2 and related viruses for the angiotensin-converting enzyme 2 receptor, which is a relatively common functional receptor in multiple organ systems.<sup>6,7</sup> Furthermore, an important complication of COVID-19 infection is thromboembolic disease and effective, even high-dose prophylaxis is required and recommended according to clinicians treating COVID-19 patients. There is

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an increasing body of evidence that blood clots are a major cause of multisystem organ dysfunction, including the respiratory failure in severe cases of SARS-CoV-2 infection.<sup>8-10</sup>

## Case Report

A 49-year-old female with multiple comorbidities including alcoholic liver cirrhosis with sequelae of portal hypertension and poorly controlled hypothyroidism presented to the hospital with worsening diffuse abdominal pain and distension over a 2-month period. Upon arrival to the emergency room, the patient was saturating 95% on 2 L of oxygen via nasal cannula and was afebrile. The patient's laboratory values were notable for acute kidney injury with creatinine of 1.5 (baseline Cr 0.9). CT of the chest, abdomen, and pelvis was performed that demonstrated cirrhotic liver and massive volume of intra-abdominal ascites. Chest CT was unremarkable, but the patient was placed under investigation for COVID-19 disease given the current high prevalence in the New York region. Nasopharyngeal swab was obtained and polymerase chain reaction (PCR) for SARS-CoV-2 initially came back negative.

On day 4 of hospitalization, the patient developed some shortness of breath, and was noted to be saturating at 91% on 2 L of oxygen via nasal cannula, which improved to 99% on nasal cannula with oxygen flow rate of 4 to 5 L. The patient otherwise remained afebrile. D-dimer was obtained and was elevated at 1,303 ng/mL. Given the patient's poor kidney function and negative chest CT 3 days earlier, nuclear ventilation-perfusion lung scan was requested.

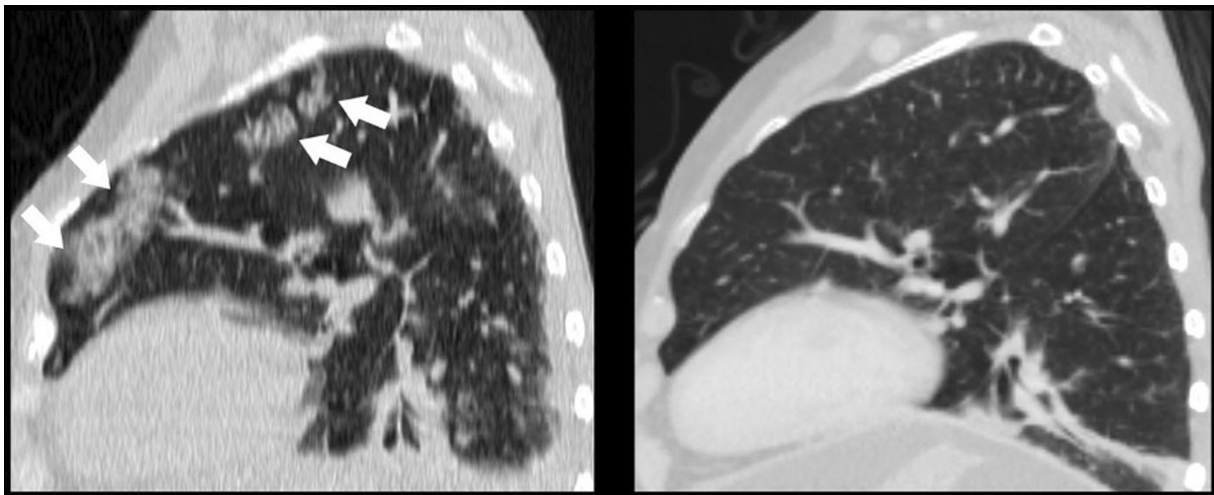
Per our institutional policy and national guidelines related to the coronavirus pandemic, the ventilation portion of the lung scan was not obtained. Instead, just lung perfusion imaging was performed using planar and single photon emission tomography/computed tomography (SPECT/CT) acquisitions.

The chest CT portion of the study demonstrated new multiple bilateral, peripheral predominant, consolidative lung opacities with reticulations typical of interstitial COVID-19 pneumonia and small pleural effusions (→ Fig. 1). The SPECT images revealed markedly abnormal lung perfusion with heterogeneous radiotracer distribution, including multiple large nonsegmental areas of reduced or absent perfusion with "stripe sign" in both lungs characteristic of lung inflammation, even without underlying parenchymal changes on corresponding CT images.<sup>11</sup> In addition, multiple subsegmental perfusion defects typical for small pulmonary emboli were also observed (→ Figs. 2 and 3). Total preserved lung perfusion function was estimated to be approximately one-third of normal function.

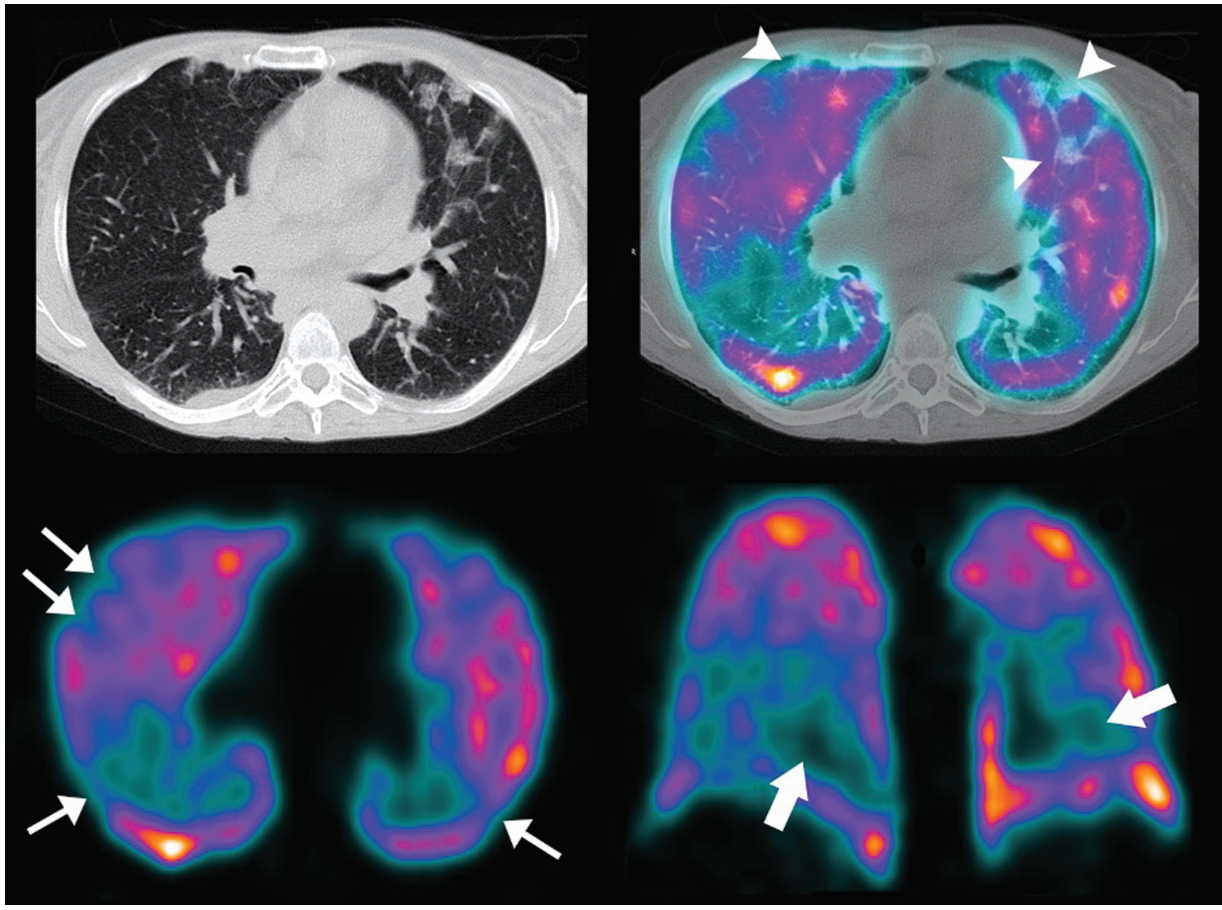
Given these findings, the patient was retested for COVID-19 and repeat PCR analysis for SARS-CoV-2 was positive.

## Discussion

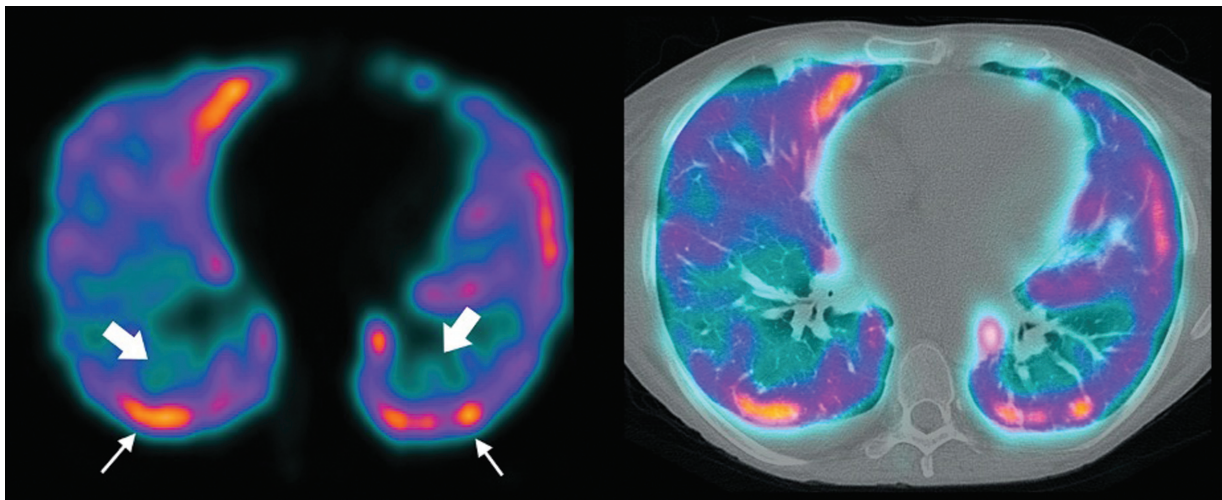
Imaging is an essential aspect of management of COVID-19 patients to evaluate the extent of different organ system involvement, severity, and progression of disease. According to recent published radiology literature, the characteristic CT findings of COVID-19 associated pneumonia most commonly include bilateral, peripheral ground-glass opacities predominantly in the lower lobes accompanied by consolidation and cavitation in more severe cases.<sup>2-4</sup> These imaging findings are nonspecific and are associated with other infectious and noninfectious inflammatory diseases.<sup>5</sup> In the current critical review, Raptis et al argue that chest CT should not be used as screening or diagnostic tool, but instead should be reserved for evaluation of complications of COVID-19 pneumonia or for assessment if alternative diagnoses are suspected.<sup>12</sup> The same conclusion was summed up in recent recommendations and position statements of several national and international organizations. Furthermore, since chest CT findings



**Fig. 1** Noncontrast chest computed tomography (CT) obtained as part of the lung perfusion single-photon emission computed tomography/computed tomography scan (*left*) in the sagittal plane (*left*) demonstrating multiple peripheral consolidative opacities (*arrows*) with air bronchograms and reticulations in the left upper lobe. These findings are characteristic of coronavirus disease 2019 pneumonia in the appropriate clinical setting. Notably, contrast-enhanced chest CT (*right*) in the sagittal plane obtained 3 days prior was unremarkable, only demonstrating subsegmental plate-like atelectasis in the left lower lobe.



**Fig. 2** Chest computed tomography (CT) (*upper left*) and single-photon emission computed tomography-computed tomography (SPECT/CT) perfusion images (*upper right*) in the axial plane at the mid lung level demonstrate multiple peripheral consolidative lung opacities with reticulation predominantly in the left upper lobe as well as the right upper lobe (*arrowheads*) with corresponding areas of decreased perfusion. A new small right-sided pleural effusion has been also developed. SPECT perfusion imaging in the axial plane (*left lower*) reveals multiple small peripheral perfusion defects (*thin arrows*) corresponding to peripheral vascular territories on CT reflecting probable small emboli. SPECT perfusion in the coronal plane (*right lower*) of the posterior lungs demonstrates large areas of central perfusion defects (*wide arrows*) not corresponding to vascular territories (“stripe sign”).



**Fig. 3** Single-photon emission computed tomography (SPECT) (*left*) and SPECT/CT perfusion images (*right*) in the axial plane near the lung bases demonstrate large areas of central perfusion defects (*wide arrows*) not reflecting vascular territories. These may represent areas of inflammation with characteristic ‘stripe sign’ (*thin arrows*) and without underlying CT abnormalities.

may be normal in up to 15% of individuals with COVID-19 infection, a normal chest CT cannot exclude the disease with certainty. However, an initial chest CT is a useful method in the rapid preliminary diagnosis of SARS-CoV-2 infection so that the suspected patient may be isolated and treated in time.<sup>13,14</sup>

Evidence has also accumulated that a subgroup of patients with severe COVID-19 disease develop cytokine storm syndrome.<sup>15,16</sup> In these cases, hyperinflammation due to rapid accumulation of T-cells and macrophages results in release of massive level of cytokines into the bloodstream aiming to destroy the offending pathogen causing numerous manifestations starting from the atypical respiratory system distress and fever, and progressing to multiorgan system dysfunction involving the heart, kidneys, and the central nervous system.<sup>17,18</sup> Thromboembolic disease giving rise to pulmonary embolism is an additional important complication of SARS-CoV-2 infection. There is apparently a causal relationship as severe inflammation and infection is a known precipitating factor for thromboembolism. Researchers in Ireland confirmed that the diffuse bilateral inflammation observed in COVID-19 is associated with significant pulmonary-specific vasculopathy that correlates with disease severity. The unexpectedly high prevalence of thromboembolism among affected patients and COVID-19 associated coagulopathy with elevated markers such as D-dimer and fibrinogen has been increasingly recognized in regions with high disease prevalence.<sup>19,20</sup> A recent study from France revealed that 30% of patients with COVID-19 infection had acute pulmonary emboli on pulmonary computed tomography angiography, a striking percentage.<sup>21</sup> Similarly, investigators from the Netherlands reported remarkably high, 31% incidence of thrombotic complications in intensive care unit patients with COVID-19 despite at least standard low-dose heparin prophylaxis.<sup>8</sup> The first series of autopsies in the United States from New Orleans showed bilateral diffuse alveolar damage with lymphocytic infiltrate predominantly in the interstitial spaces and fibrin thrombi within the capillaries and small vessels throughout the lungs.<sup>22</sup> Reported autopsy results from Italy indicate that in addition to diffuse inflammatory infiltrate, major relevant lung finding is the presence of platelet-fibrin thrombi in small arterial vessels that is important in the clinical context of coagulopathy dominating the clinical course in these patients.<sup>23</sup>

While elevated D-dimer is a frequent finding in COVID-19 infection, it is not specific for the diagnosis of venous thromboembolism.<sup>15</sup> On the other hand, CT angiography may contribute to, or even cause development of acute kidney injury in these patients already at risk of renal failure. Therefore, consideration should be given to lung perfusion radionuclide scan as the preferred imaging modality when pulmonary embolism is suspected in SARS-CoV-2 patients. Furthermore, based on the presented case we postulate that functional abnormalities evident as widespread perfusion reduction on radionuclide perfusion tomographic images may precede abnormal morphological findings on chest CT in some patients. The extent of abnormal perfusion defects likely reflects widespread lung inflammation and multiple small thromboemboli without corresponding structural damage on

CT images was an unexpected finding in the presented case of patient with COVID-19 pneumonia. These findings are in accordance with the reported clinical course of disease and underlying pathological findings. This patient had multiple comorbidities and there are other possible explanations for the perfusion defects including vascular and oxygenation changes from a pulmonary manifestation of cirrhosis or portal hypertension, as well as long-term lung damage and possible autoimmune disease linked to the poorly controlled hypothyroidism. Chest CT remains an important initial imaging approach in COVID-19 patients with the addition of CT angiography when thromboembolism is suspected. Functional perfusion imaging in combination with low-dose CT (SPECT/CT) is an alternative study in COVID-19 patients when thromboembolism is suspected. In addition, SPECT/CT perfusion imaging may visualize and assess early lung parenchymal changes caused by interstitial pneumonia and related comorbidities such as pulmonary embolism, pulmonary hypertension, and heart failure.<sup>11</sup> In institutions without a SPECT/CT camera, SPECT imaging alone may be useful especially if it can be fused with chest CT for correlation.

## Conclusion

Comorbidity of pneumonia and pulmonary embolism is a frequent finding in COVID-19 infection. Although chest CT is the mainstay for the evaluation of these lung pathologies, hybrid SPECT/CT imaging technology can be useful as an adjunct or alternative study. Lung perfusion SPECT/CT may identify pulmonary embolism including small subsegmental emboli, as well as parenchymal lung changes on underlying chest CT images in patients with COVID-19 disease. In this case study, we showed extensive SPECT/CT nonsegmental defects that we hypothesize may indicate an early lung involvement or inflammatory changes in SARS-CoV-2 infection.

This imaging approach should be considered in the management of COVID-19 patients, and further evaluated in well-planned prospective clinical studies.

### Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for the images and other clinical information to be reported in this journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

### Note

The work was carried out at the Department of Radiology at Stony Brook University Hospital.

### Funding

None.

### Conflicts of Interest

None declared.

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