RESEARCH ARTICLE

# Vascular enlargement and bronchiolectasis: Two important CT manifestations in Coronavirus Disease 2019 (COVID-19) and clinicopathologic analysis

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**Coronavirus disease 2019 (COVID-19) is a novel infectious disease that spreads rapidly around the world and endangers global public health. Because of the lack of specificity of previously identified CT images, such as peripheral and subpleural ground glass opacities, early diagnosis is still a big challenge for radiologists. How to improve the accuracy of diagnosis and make diagnosis as early as possible is a problem concerned by the medical field. This article reports two important CT manifestations in COVID-19 patients, and investigates the pathogenesis and clinical significance of them. Single or multiple CT scans in COVID-19 patients confirmed at our hospital were retrospectively analyzed. The presence of vascular enlargement sign and bronchiolectasis sign on CT images were evaluated with the help of sophisticated post-processing techniques. A total of 14 patients (6 men and 8 women; mean ±standard deviation age: 41.51 ±20.98 years) with 34 CT series were included. Vascular enlargement sign at a distribution of interior or the edge of pulmonary lesions was observed in all CT series (34/34, 100%). Bronchiolectasis sign was observed in 30 CT series (88%), with 4 series (4/7, 57.1%) in early stage, 16 series (16/16, 100%) in progressive stage, 5 series (5/5, 100%) in severe stage and 9 series (9/9, 100%) in absorption stage. The occurrence of bronchiolectasis sign in COVID-19 patients was significantly different between early stage and non-early stage (P=0.005). This study suggests that the vascular enlargement sign and bronchiolectasis sign are two important CT features in COVID-19 patients and may be of great significance in early diagnosis and guiding treatment decisions.**

***Keywords:*** COVID-19, CT imaging, Early diagnosis, Treatment

***Abbreviations:*** COVID-19, Coronavirus Disease 2019; WHO, World Health Organization; CT, computed tomography; GGO, ground-glass opacity; RT-PCR, real-time reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; MERS, Middle East respiratory syndrome; ARDS, acute respiratory distress syndrome.

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## Introduction

In December, 2019, a series of coronavirus disease 2019 (COVID-19) cases emerged. Since then, the disease has spread rapidly around the world, and was declared as a global health emergency of world concern by World Health Organization (WHO) on February 11, 2020[1-4]. Common symptoms of COVID-19 include fever, dry cough, and fatigue[5,6]. As of early June, 2020, accumulatively six million cases with COVID-19 have been confirmed globally, of whom 370,000 died[7]. According to the *Diagnosis and Treatment Plan for New Coronavirus Infected Pneumonia (Sixth Edition)*, radiologic findings, especially computed tomography (CT) manifestations, are of great significance in diagnosis and guiding therapeutic strategy[8].

Previous studies indicated that unilateral and bilateral peripheral lung distributions of ground-glass opacity (GGO) is a typical imaging manifestation of early-stage COVID-19, but some radiologists believe that other types of pneumonitis may also have this feature[9,10]. With the accumulation of cases, a wider spectrum of radiologic findings has been reported, including crazy paving pattern, halo sign, reversed halo sign, cavity, etc[11-14]. In particular, we noticed the occurrence of vascular enlargement and bronchiolectasis in many COVID-19 cases, may be helpful for early diagnosis and guiding treatment. However, the two signs have not been reviewed comprehensively with regard to the pathology and pathophysiology.

Therefore, in this retrospective study, we reported in detail the two important CT manifestations in COVID-19 patients, vascular enlargement sign and bronchiolectasis sign, and investigated their pathogenesis and clinical significance in combination with the latest autopsy pathology reports. CT post-processing was also performed to reconstruct images for better visualization of these signs, thereby increasing correct diagnoses.

## Patient and Method

This retrospective study was approved by local Ethics of Committee. Patient inclusion criteria were as follows: (a) Patients had a positive result of real-time reverse transcription polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); (b) Patients underwent a single or multiple thin-section CT examinations at our hospital; (c) CT scans showed pulmonary abnormalities. From January 23, 2020 to February 15, 2020, 15 patients were consecutively employed. One patient was excluded for only having a single CT scan with normal result. The remaining 14 patients were finally included.

## CT Protocol and Image Reconstruction

Unenhanced chest CT examination was performed in a 64-row, 128-section spiral scanner (Siemens Somatom Perspective, Germany) with the following parameters: tube voltage, 80/100kV; tube current, 50 mAs; CARE Dose, on; rotation time, 0.6 s; pitch, 1.45; section thickness, 5 mm; section interval, 5 mm; collimator, 64 × 0.6 mm; and matrix, 512 × 512. Images were reconstructed using the iterative reconstruction technique with a thickness of 1 mm and an interval of 0.7 mm. All images were transferred to Siemens workstation (syngo.via, version 4.1) and post-processed by using the PULMO 3D software (VB20, Siemens Healthineers, Forchheim, Germany). In the reconstructed two-dimensional images, pulmonary parenchyma and vessels were differentiated by CT values and highlighted in different pseudo-colors.

## Image Interpretation

All CT images were independently reviewed and analyzed by two senior radiologists, each with more than 10 years of experience in thoracic imaging diagnosis. A third radiologist (more than 20 years of experience) would be consulted and make the final decision when disagreement occurred. The following CT indicators were evaluated: (a) vascular enlargement sign, defined as the presence of dilated blood vessels in or around pulmonary lesions; (b) bronchiolectasis sign, defined as the dilated bronchioles in or around pulmonary lesions; and (c) disease severity based on radiologic findings: early stage, progressive stage, severe stage and absorptive stage [10].

## Statistical Analysis

All data were analyzed with Pearson's chi-squared test (categorical variables) or Fisher's exact test using SPSS software (version 24.0, SPSS Inc, Chicago, IL, USA). Two-tailed $P$ values of < 0.05 were considered statistically significant.

## Results

**Table 1** Patient characteristics

| | COVID-19 patients |
|---|---|
| **All** | 14 |
| **Sex** | |
| Male | 6 (43%) |
| Female | 8 (57%) |
| **CT scans** | |
| Once | 2 (14%) |
| Twice | 6 (43%) |
| Three times | 1 ( 7%) |
| Four times | 5 (36%) |
| **Lung changes** | |
| Early stage | 7 (19%) |
| Progressive stage | 16 (43%) |
| Severe stage | 5 (14%) |
| Absorption stage | 9 (24%) |

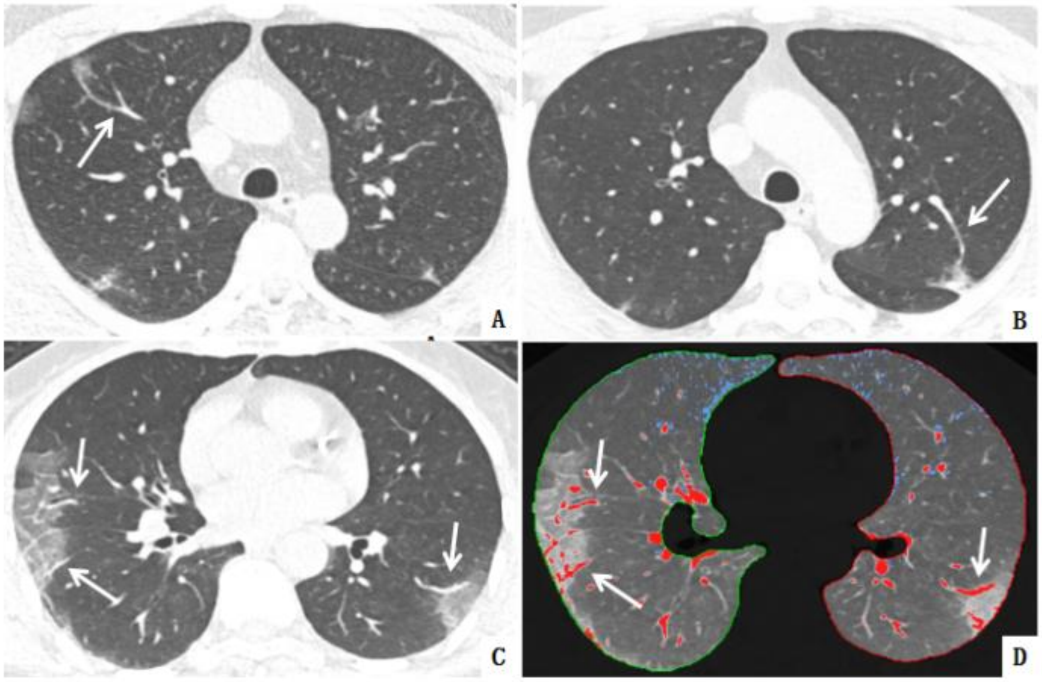


**Figure 1. The vascular enlargement sign.** (A, B, C) Axial thin-section unenhanced CT shows vascular enlargement (white arrows) in or around the ground-glass opacities.(D) PULMO-3D reconstructed images of C with highlight of enlarged vessels.

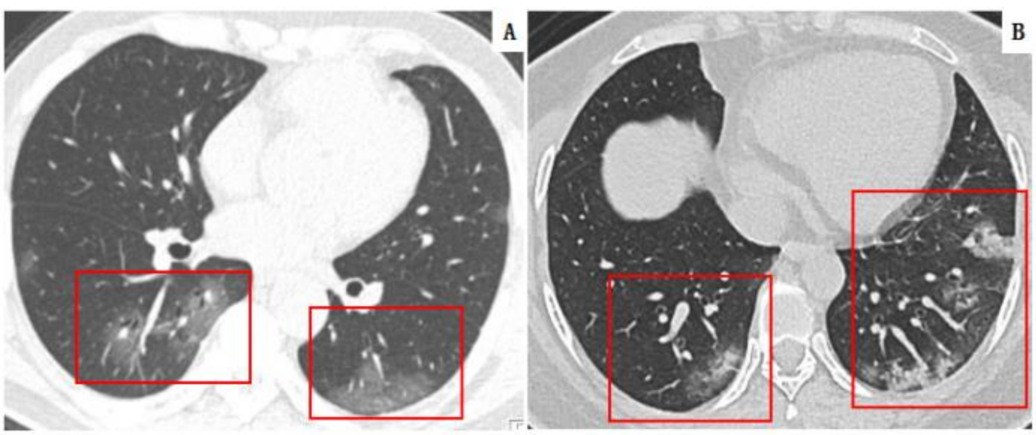


**Figure 2. The vascular enlargement sign and bronchiolectasis sign.** (A, B) Axial thin-section CT scans show simultaneous vessels and bronchioles dilatation in the ground glass opacities (red frames). The diameter of the dilated distal bronchioles is equal to or less than that of the adjacent dilated vessels.

A total of 34 CT scans (mean interval: 3.78 days, range: 2-7 days) from 14 patients (6 males and 8 females; 41.51 ±20.98 years) were assessed (Table 1).

### Clinical and Laboratory Findings

Of the 14 patients, two had hypertension, one had chronic bronchitis, one had myocardial ischemia, and the other 10 cases had no special medical history. Nine patients (64%) had a history of traveling or living in Wuhan, and five patients (36%) had close contacts with people from Hubei Province, China. The most common clinical symptoms were fever (11/14, 79%) and cough (11/14, 79%), and three patients had normal body temperature. Other symptoms included fatigue, runny nose, chest tightness, palpitation, and shortness of breath.

The blood counts showed normal white blood cell count

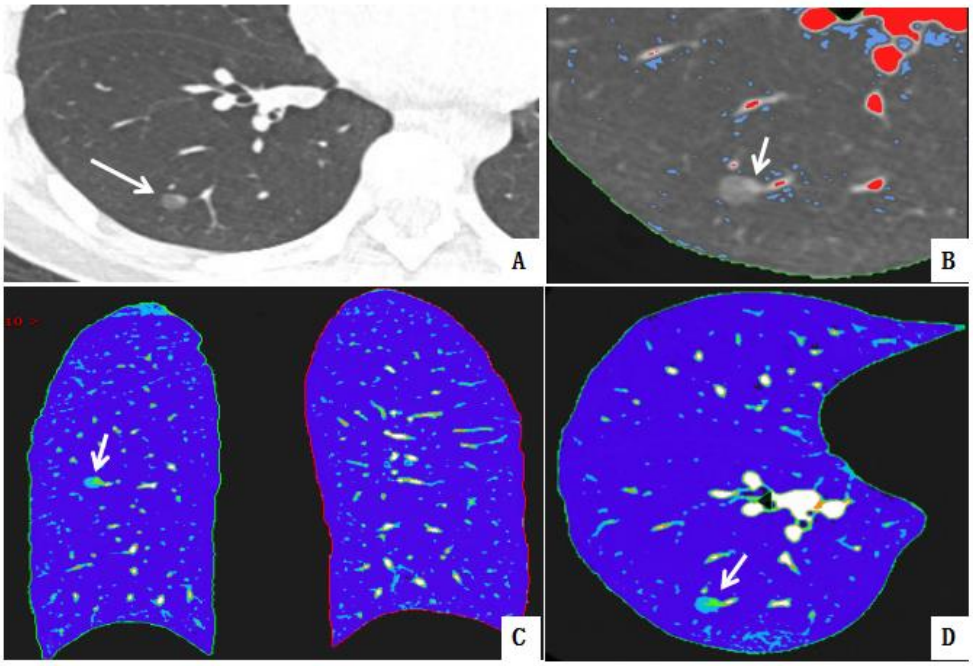


**Figure 3. A 34-year-old female patient with COVID-19 in early stage.** (A) Axial thin-section unenhanced CT scan shows a single ground-glass nodule. (B, C, D) PULMO-3D reconstructed images show vascular enlargement more clearly (white arrows).

(10/14, 71%) and low lymphocyte levels (8/14, 57%) in most patients. C-reactive protein was increased in 10 cases (71%), and sedimentation rate was elevated in 8 cases (57%). Elevations of creatinine, lactate dehydrogenase, creatine kinase and D-dimer were shown in some patients. Twelve patients (86%) were tested positive in the first RT-PCR assay for detecting COVID-19 using nasopharyngeal swab. One patient was tested negative in the first two pharynx swab tests and positive in the third alveolar lavage fluid test. Two patients (14%) had positive results in anal swab RT-PCR tests. Other samples, such as milk and urine, were not detected with COVID-19 nucleic acid.

## CT Imaging Findings

### *Presence and distribution of ground glass opacities*

Of the 14 initial chest CT scans, one (7%) presented with a single ground glass nodule with a diameter of 10 mm, one (7%) presented with a rounded mass shadow, and the other 12 cases (86%) presented with multiple ground glass opacities in bilateral lungs. All lesions were distributed mainly in the outer pulmonary field or subpleura. Pulmonary lobe involvement included one-lobe involvement in one case (7%), three-lobe involvement in 3 cases (21%), four-lobe involvement in 2 cases (14%), and five-lobe involvement in 8 cases (58%). A total of 58 lung lobes were involved, including 12 cases (21%) in the upper lobe of the left lung, 12 cases (21%) in the lower lobe of the left lung, 11 cases (19%) in the upper lobe of the right lung, 9 cases (15%) in the middle lobe of the right lung, and 14 cases (24%) in the lower lobe of the right lung.

With regard to illness assessment, the initial CT scans showed early stage of disease in 5 patients (36%), severe stage in 2 (14%), and progressive stage in 7 (50%). During hospitalization, 12 patients received two or more CT examinations to monitor disease progression. Four patients (28%) became worse in a short time, presenting with enlarged scope and volume of lesions in the bilateral lungs, and one of them had a 10-year history of chronic bronchitis. One patient (7%), aged 59 years, showed disease progression again after the improvement of absorption. Two severe cases (14%), who had hypertension and myocardial ischemia, respectively, improved slowly, presenting with multiple large flakes of ground-glass shadows and consolidation foci in the lungs. One patient did not show disease progression (7%), and 4 patients showed gradual absorption of lesions (28%).

Other abnormalities were also seen in some patients, including 1 patient (7%) with two calcification nodules in the upper lobe of the right lung, 1 patient (7%) with a lung mass in the lower lobe of the right lung, and 3 patients (21%) with chronic fibrosis in the lungs. Meanwhile, mild bilateral pleural effusion was found in one case (7%), and no enlargement of mediastinal or hilar lymph nodes was found.

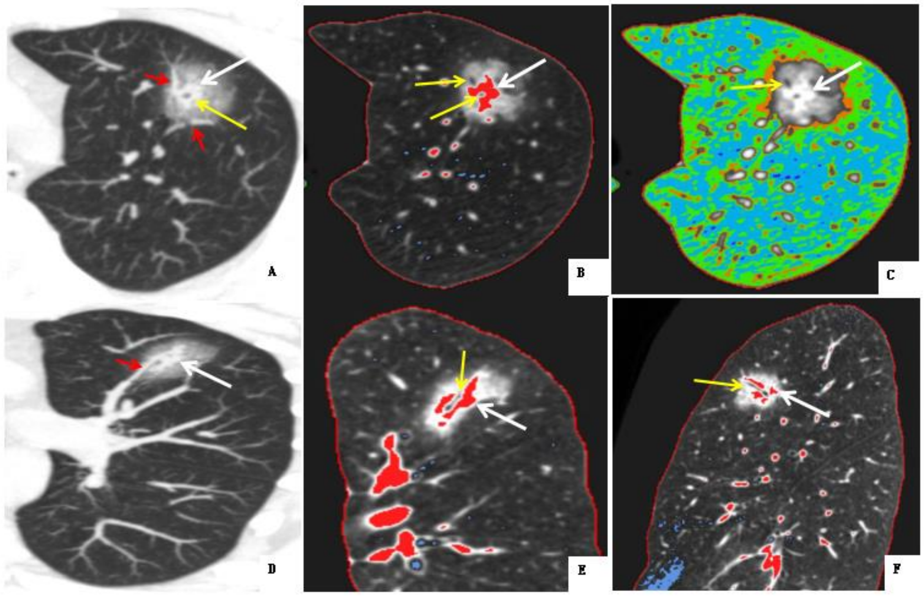


**Figure 4. A 33-year-old male patient with COVID-19 in early stage.** (A) Axial thin-section unenhanced CT shows a rounded ground-glass opacity with vascular enlargement and bronchiolectasis sign (vascular enlargement in red arrows and bronchiolectasis in yellow arrow) and patchy high density area (white arrow). (B,C) PULMO-3D reconstructed images clearly show dilated bronchioles (yellow arrows)and suspected intra-focal hemorrhage (white arrow). (D) Maximum intensity projection (MIP) reconstruction. (E,F) Coronal and sagittal PULMO-3D reconstruction images clearly show dilated bronchioles (yellow arrow) and suspected intra-focal hemorrhage (white arrow).

### *The vascular enlargement sign and bronchiolectasis sign*

Vascular enlargement sign was observed in all CT series (34/34, 100%), which was mainly distributed at the interior or the edge of ground-glass shadows and consolidated areas A representative image is shown in Figure 1. In conventional thin-slice CT images, vascular enlargement sign in small lesions may be not recognized without pseudo-color reconstruction (Figure 3). Moreover, bronchiolectasis sign (Figures 2 and 4) was observed in most series (30/34, 88%), including 4 series (4/7, 57.1%) at the early stage, 16 series (16/16, 100%) at the progressive stage, 5 series (5/5, 100%) at the severe stage and 9 series (9/9, 100%) at the absorption stage. The incidence of bronchiolectasis sign in COVID-19 patients differed significantly between early-stage and other stages ($p$ =0.005).

## Discussion

The number of COVID-19 infections is still increasing since the outbreak, and has become a great threat to global public health [15-17]. Consistent with the previous literature, most of our cases (12 of 14, 86%) presented with multiple GGO in the peripheral and subpleural zone of unilateral or bilateral lungs. However, two cases in this report presented with a single ground glass nodule (Figure 3) and a rounded mass shadow (Figure 4), which are difficult to be differentiated from other lesions such as pure ground-glass nodule, other types of pneumonia, and inflammatory pseudotumor. At the early stage of disease, it may be a big challenge for radiologists to identify these atypical CT findings and make correct diagnosis. Yet, in our study, we found two important CT imaging features, vascular enlargement sign and bronchiolectasis sign, which may be helpful for early diagnosis and differential diagnosis of COVID-19 pneumonia. Moreover, the reconstruction techniques of PULMO 3D software are helpful to identify these two signs in pulmonary lesions.

Initially, pathologists performed needle sampling from a COVID-19 cadaver, and the local histopathological changes of COVID-19 were very similar to those of SARS and Middle East respiratory syndrome (MERS). The bilateral diffuse alveolar damage with fibromyxoid exudates, transparent membrane formation and pulmonary edema, is indicative of acute respiratory distress syndrome (ARDS) [18-20]. On February 16, 2020, Liu *et al.* performed a systematic autopsy on a COVID-19 cadaver. Gross anatomy showed pulmonary venous congestion with focal hemorrhage. Some lung lobules expanded and turned white, mixed with dark red areas of congestion and hemorrhage, mainly distributed in the outer field of the lung. After incision, a large amount of offwhite mucus flew out, the trachea cavity was filled with white foam mucus, and the gelatinous mucus was attached to the bronchial lumen [21].

The complete pathological findings were published in the *Diagnosis and Treatment Plan for New Coronavirus Infected Pneumonia* (seventh edition) on March 4, 2020[22]. These include presence of serous fluid, fibrin exudate and transparent membrane in alveoli; significant proliferation of type II alveolar epithelial cells, with virus inclusion bodies thereof; alveolar septal vessels showing hyperemia, edema, inflammatory cell infiltration, and transparent thrombus formation; occurrence of focal hemorrhage, necrosis, and hemorrhagic infarction in the lung tissues; partial fall off of the bronchial mucosa, with formation of mucus and mucus embolus in cavity; presence of coronavirus particles in the cytoplasm of bronchial mucosal epithelial and type II alveolar epithelial cells under electron microscopy; and COVID-19 antigen-positive alveolar epithelium cells and macrophages as evidenced by immunohistochemistry. These pathological findings can explain the CT imaging alterations of COVID-19.

The inflammation starts from bronchi and bronchioles, and develops along the interstitium of the lungs. The alveolar septa are widened, with no exudation or little exudation in the alveolar cavity. At this point, chest CT may reveal no special changes, and the patient may be asymptomatic or only have mild symptoms.

As the disease progresses, bronchi, bronchioles and surrounding capillaries were further burdened with congestion and edema, due to the infiltration of inflammatory cells. The bronchial tube wall and alveolar wall undergo denaturation, necrosis and exudation, and severe inflammatory exudation occurs in the alveolar cavity. Thus, the peripheral GGO appears on CT imaging, which indicates the early stage of COVID-19. This completely corresponds to the offwhite alveolar lesions seen in the gross anatomy, suggesting that COVID-19 mainly causes an inflammatory response characterized by damage to the distal small airway and alveoli[21].

At the early or progressive stage, dilated blood vessels appear in or around the GGOs, which is the so-called vascular enlargement sign. Zhao et al. proposed that the vascular enlargement may be caused by acute inflammatory responses, and suggested that its feature of being distributed in the peripheral lung could be used to distinguish COVID-19 from lung adenomas which are characterized by thickened blood vessels [23]. In our study, however, we found that these dilated vessels originate from the veins, which is consistent with the pulmonary congestion seen from gross anatomy. We speculate that there may be transparent thrombosis in the venule lumen, causing local obstruction and then dilation of the distal vessels. Furthermore, there were patch-like high-density shadows in some lesions (Figure 4), consistent with the vascular density, especially in the reconstructed images of PULMO 3D. We considered the high-density shadows to be a focal hemorrhagic lesion. The thickening and dilatation of small vessels in the lesion area may cause damage to the vascular endothelium, resulting in increased permeability, even rupture and bleeding of the vessel wall. In addition, the CT post-processing techniques revealed a vascular dilatation sign within a 10-mm small ground-glass nodule in this series of cases (Figure 3), suggesting that this sign could be used to guide early diagnosis of COVID-19.

In this study, we found presence of dilated bronchioles in or around pulmonary lesions, namely, bronchiolectasis sign. The diameter of the dilated distal bronchioles was similar or smaller than that of the adjacent dilated vessels. This sign was referred to as air bronchogram and tractive bronchiectasis in previous studies[24-26]. However, as they are more commonly seen in pulmonary consolidation and late period of inflammation, respectively, bronchiolectasis occurs more specifically at the early or progressive stage of COVID-19. From the time window of the three signs, the bronchiolectasis sign of COVID-19 has an earliest occurrence. Since gross anatomy revealed a large amount of mucus in the lung tissue, trachea and bronchial lumen after incision, we speculated that the bronchiolectasis sign may be associated with mucus attachment or partial lumen obstruction. This explains why most patients present with dry cough and no sputum. Therefore, the appearance of bronchiolectasis sign may indicate the formation of mucus embolus in the bronchial lumen. Clinicians should pay more attention to this sign and take further measures to dilute sputum and promote sputum elimination (e.g., sputum aspiration, sputum medication, etc.), thus preventing worsening of the disease.

In severe cases, due to extensive denaturation and necrosis of bronchi and alveolar wall, and the formation of transparent membrane, pulmonary foci are enlarged substantially, lungs become consolidated, even white lung signs appear. In this period, due to the high density of consolidated lung tissues, the vascular enlargement and bronchiolectasis signs cannot be clearly displayed on conventional thin-slice CT images, but post-processing techniques can facilitate better visualization of these signs in patients. Due to the large amount of jelly-like phlegm obstruction in peripheral lung tissue and poor drainage of pulmonary secretions, the ventilation function of respiratory pulmonary lobule is seriously impaired, causing significant decrease of oxygenation index of the patients. During this period, hypoxia may hardly be reversed even if patients are given adequate oxygen therapy. Therefore, early identification of bronchiolectasis is of great significance in guiding clinical treatment.

**Limitations**

There are some limitations in this study. First, the number of patients was relatively small, and some patients did not undergo follow-up CT examination. Seven patients only had one follow-up CT in the study window. Second, the pathophysiological mechanism of COVID-19 is still under investigation. Our analysis of the vascular enlargement and bronchiolectasis signs is based on the pathological findings of COVID-19 autopsy and the knowledge on pathogenesis of ARDS, so further clinicopathological studies are needed for verification. Third, the two signs have been seen in some cases of SARS and MERS[23-25], thus may be a specific sign for coronavirus pneumonia (especially COVID-19). Large-sample comparative studies are needed for clarification.

## Conclusion

Vascular enlargement and bronchiolectasis are two important CT signs of COVID-19 pneumonia, which begin to appear at the early or progressive stage of the disease. Recognition and familiarity with these signs could help radiologists make diagnosis as early as possible, which is of great significance for controlling the spread of the disease. The appearance of bronchiolectasis sign indicates the formation of mucus embolus in the bronchial lumen, which may have certain guiding significance for clinical treatment.

## Ethics Approval

This study was approved by the ethics committee of Guizhou Provincial People's Hospital.

## Patient Consent for Publication

All patients were informed of the purpose and methods of the study and signed individual informed consent forms.

## Conflicting Interests

The authors declare that they have no conflicts of interest.

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