# Chest computed tomography analysis of lung sparing morphology: differentiation of COVID-19 pneumonia from influenza pneumonia and bacterial pneumonia using the arched bridge and vacuole signs

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## ABSTRACT

**Introduction:** This study evaluated the arched bridge and vacuole signs, which constitute morphological patterns of lung sparing in coronavirus disease 2019 (COVID-19), then examined whether these signs could be used to differentiate COVID-19 pneumonia from influenza pneumonia or bacterial pneumonia.

**Methods:** In total, 187 patients were included: 66 patients with COVID-19 pneumonia, 50 patients with influenza pneumonia and positive computed tomography findings, and 71 patients with bacterial pneumonia and positive computed tomography findings. Images were independently reviewed by two radiologists. The incidences of the arched bridge sign and/or vacuole sign were compared among the COVID-19 pneumonia, influenza pneumonia, and bacterial pneumonia groups.

**Results:** The arched bridge sign was much more common among patients with COVID-19 pneumonia (42/66, 63.6%) than among patients with influenza pneumonia (4/50, 8.0%; P<0.001) or bacterial pneumonia (4/71, 5.6%; P<0.001). The vacuole sign was also much more common among patients with COVID-19 pneumonia (14/66, 21.2%) than among patients with influenza pneumonia (1/50, 2.0%; P=0.005) or bacterial pneumonia (1/71, 1.4%; P<0.001). The signs occurred together in 11 (16.7%) patients with COVID-19 pneumonia, but they did not occur together in patients with influenza pneumonia or bacterial pneumonia. The arched bridge and vacuole signs predicted COVID-19 pneumonia with respective specificities of 93.4% and 98.4%.

**Conclusion:** The arched bridge and vacuole signs are much more common in patients with COVID-19 pneumonia and can help differentiate COVID-19 pneumonia from influenza and bacterial pneumonia.


Hong Kong Med J 2023;29:39–48
https://doi.org/10.12809/hkmj219291

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**New knowledge added by this study**

- On computed tomography, the arched bridge sign is characterised by ground-glass opacities or consolidation with an arched margin outlining unaffected lung parenchyma. The vacuole sign refers to a focal oval or round lucent area (typically <5 mm) that is present within ground-glass opacities or sites of consolidation.
- These signs were commonly observed in patients with coronavirus disease 2019 (COVID-19) in Hong Kong, consistent with data from other populations.
- Patients with COVID-19 pneumonia are much more likely to exhibit the arched bridge sign and/or the vacuole sign, compared with patients who have influenza pneumonia or bacterial pneumonia.

**Implications for clinical practice or policy**

- The presence of the arched bridge sign and/or the vacuole sign on computed tomography may support a diagnosis of COVID-19 pneumonia and assist in differentiation from other types of pneumonia.
- The duration of total hospitalisation did not differ between patients with COVID-19 pneumonia who had and did not have these two signs, suggesting that they do not indicate a better or worse prognosis if appropriate treatments are administered.

  

## 肺組織保留表現的胸部電腦斷層分析：利用拱形橋徵和空泡徵區分2019冠狀病毒肺炎與流感性肺炎或細菌性肺炎

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**目的**：拱形橋徵和空泡徵提示2019冠狀病毒肺炎中肺組織保留的形態學表現。本研究評估這兩個徵象，並探討是否有助區分2019冠狀病毒肺炎、流感性肺炎或細菌性肺炎。

**方法**：本研究共納入187例患者，包括66例2019冠狀病毒肺炎患者、50例電腦斷層呈陽性結果的流感肺炎患者及71例電腦斷層呈陽性結果的細菌性肺炎患者。兩名放射科醫生獨立閱讀電腦斷層圖像。本研究並比較2019冠狀病毒肺炎、流感性肺炎和細菌性肺炎組的拱形橋徵及／或空泡徵的出現頻率。

**結果**：與流感性肺炎（4/50，8.0%；P<0.001）或細菌性肺炎（4/71，5.6%；P<0.001）相比，在2019冠狀病毒肺炎中觀察到拱形橋徵的頻率更高（42/66，63.6%）。與流感性肺炎（1/50，2.0%；P=0.005）或細菌性肺炎（1/71，1.4%；P<0.001）相比，在2019冠狀病毒肺炎中觀察到空泡徵的頻率也更高（14/66，21.2%）。這兩個徵象在11例（16.7%）2019冠狀病毒肺炎患者中同時出現，但在流感性肺炎或細菌性肺炎患者中則未同時出現。在本研究中，拱形橋徵和空泡徵提示2019冠狀病毒肺炎的特異性分別為93.4%和98.4%。

**結論**：拱形橋徵和空泡徵在2019冠狀病毒肺炎患者中更為常見，有助區分2019冠狀病毒肺炎與流感性肺炎或細菌性肺炎。


## Introduction

A diagnosis of coronavirus disease 2019 (COVID-19) is made on the basis of epidemiological and clinical history, as well as the results of severe acute respiratory syndrome coronavirus 2 real-time reverse transcriptase polymerase chain reaction (RT-PCR) testing. Chest computed tomography (CT) has been proposed as a useful alternative investigation method for COVID-19 diagnosis or triage, particularly in healthcare settings with restricted access to RT-PCR testing and in the context of lower RT-PCR sensitivity during early stages of the disease; it may also be useful for imaging-mediated evaluation of disease severity and progression.[1,2] The most common CT findings in early-stage COVID-19 pneumonia (illness days 0-5) are pure ground-glass opacities (GGOs); the second most common finding is consolidation.[3,4] In the later stages (illness days 6-17), findings usually evolve to a combination of GGOs, consolidation, and reticular opacities with architectural distortion.[4] These imaging features are not specific to COVID-19 pneumonia; they can overlap with other types of viral or bacterial pneumonia, particularly influenza pneumonia, as well as other non-infectious inflammatory lung diseases.[5,6] Influenza, one of the most common causes of viral pneumonia,[7] and bacterial pneumonia, historically the most common type of community-acquired pneumonia worldwide,[8] maintained high incidences during the early COVID-19 pandemic when this study was conducted; thus, they had the potential to substantially contribute to hospitalisations in this period. However, COVID-19 pneumonia and other types of viral or bacterial pneumonia distinctly differ in terms of their disease course, temporal progression, and available therapeutics[9-11]; thus, there is a need for early and accurate differentiation among these entities.

Studies in 2020 revealed several CT imaging features that can aid in differential diagnosis. Compared with influenza pneumonia, patients with COVID-19 pneumonia are more likely to exhibit a peripheral distribution,[12-14] patchy combination of GGOs and consolidation,[15] fine reticular opacities,[16] and vascular thickening or enlargement[16,17]; patients with influenza pneumonia are more likely to exhibit nodules,[18] tree-in-bud sign,[18] bronchial wall thickening,[15] lymphadenopathy,[16] and pleural effusions.[12] In the past, diffuse airspace consolidation, centrilobular nodules, bronchial wall thickening, and mucous impaction[19] have been identified as typical signs of bacterial pneumonia. Nevertheless, CT assessment of COVID-19 generally remains challenging, with reported accuracies for radiologists ranging from 60 to 83%[16] in terms of differentiating patients with COVID-19 pneumonia from patients with influenza pneumonia; considering these rates, further studies of relevant imaging findings are needed.

A report by Wu et al[20] highlighted the arched bridge sign, which may be a distinct CT feature of COVID-19 pneumonia. In their analysis of 11 patients with COVID-19 pneumonia, the sign was present in 72.7%.[20] The arched bridge sign refers to a specific pattern of GGOs or consolidation, commonly in a subpleural location, which forms an arched contour with a smooth concave margin towards the pleural side. The arched margin outlines the spared parenchyma between the GGOs or consolidation and the pleural surface. Another reported sign, regarded as the vacuole sign,[21-24] is presumably based on the morphological pattern of parenchymal sparing in areas of affected lung. The vacuole sign refers to a focal oval or round lucent area (typically <5 mm) that is observed within GGOs or sites of consolidation. In clinical practice, we often observed these two novel signs on CT scans of patients with COVID-19 pneumonia. We hypothesised that these two signs are common in patients with COVID-19 pneumonia and thus could be used to differentiate such pneumonia from other types of infection-related pneumonia. However, considering the limited prior evidence (solely from small retrospective studies[20-24]) regarding the prevalence of the vacuole sign in COVID-19 pneumonia, and because the arched bridge sign has—to our knowledge—only been reported in a single previous publication,[20] additional assessments of these signs are needed. The utilities of the arched bridge and vacuole signs in COVID-19 pneumonia have not been directly assessed in prior reports, nor have they been compared between COVID-19 pneumonia and other types of infection-related pneumonia. In this study, we evaluated the arched bridge and vacuole signs in patients with COVID-19 pneumonia, then examined whether these signs could be used to differentiate such pneumonia from influenza pneumonia or bacterial pneumonia.

# Methods

## Patients

This retrospective study included consecutive patients who were admitted to two hospitals in Hong Kong (Prince of Wales Hospital and Princess Margaret Hospital) with RT-PCR–confirmed COVID-19, along with positive CT findings, from 24 January 2020 to 16 April 2020. These patients represent most patients with COVID-19 in Hong Kong during the study period, when all patients with confirmed COVID-19 were hospitalised regardless of clinical status; moreover, Princess Margaret Hospital also served as a centralised treatment centre for patients with COVID-19. The study recruitment period reflects the early days of the COVID-19 pandemic in Hong Kong, during which CT examinations were commonly performed during the diagnosis and treatment of patients with COVID-19. All patients with COVID-19 underwent complete PCR-based assessment of multiple respiratory pathogens on admission; patients with COVID-19 were excluded from the present study if they exhibited evidence of other concomitant viral or bacterial respiratory infections.

The influenza pneumonia and bacterial pneumonia comparison groups comprised consecutive patients who were admitted to Prince of Wales Hospital in Hong Kong, with pure influenza pneumonia or pure bacterial pneumonia and positive CT findings from 20 February 2018 to 13 January 2020. The diagnosis of pure influenza pneumonia was determined by RT-PCR–mediated detection of influenza A or B viral RNA, in the absence of evidence (eg, respiratory or blood cultures, PCR tests, or serological tests) suggesting concomitant infection with other viral or bacterial pathogens. The diagnosis of pure bacterial pneumonia was determined by positive bacterial culture on sputum or bronchoalveolar lavage, in the absence of evidence suggesting concomitant infection with other viral or bacterial pathogens. Patients with pre-existing lung parenchymal disease (eg, interstitial lung disease) or known lung malignancy were excluded from the study.

## Image acquisition

Computed tomography scans were performed using 64-section multidetector scanners (LightSpeed VCT or LightSpeed Pro 32, GE Medical Systems, Milwaukee [WI], United States). The following scan parameters were used: voltage, 120 kV; tube current, 50-502 mA; and slice thickness, 0.625 mm or 1.25 mm. Scans were performed with the patient in the supine position during end-inspiration.

## Image evaluation

All CT images were reviewed in random order by two trained radiologists (TY So and YX Wang) with 7 and 5 years of experience in diagnostic chest imaging, respectively, using a dedicated picture archiving and communication system workstation. Each radiologist was blinded to demographic and clinical information for all patients. The images were independently reviewed by each radiologist, and the consensus findings for any discrepancies from discussion are reported.

Each CT image was initially subjected to broad assessment of abnormalities. Subsequently, the arched bridge and vacuole signs were specifically assessed; the presence or absence of each sign was recorded. The arched bridge sign was defined as the presence of GGOs or consolidation with an arched concave margin outlining a region of spared lung; the vacuole sign was defined as the presence of a vacuole-like region of normal lung (<5 mm) within GGOs or sites of consolidation.[21]

For patients with COVID-19 pneumonia and patients with influenza pneumonia, CT findings of GGOs (hazy areas of parenchymal opacities that did not conceal underlying vessels), consolidation (parenchymal opacities that concealed underlying vessels), reticular opacities (coarse linear or curvilinear opacities, interlobular septal thickening, or subpleural reticulation), and crazy paving pattern (GGOs with interlobular and intralobular septal thickening) were recorded. Other signs such as air bronchograms (air-filled bronchi on a background of opaque lung), nodules (small rounded focal opacities <3 cm), cavitation (gas-filled spaces within sites of pulmonary consolidation), bronchiectasis, pleural retraction or thickening, pleural effusion, pericardial effusion, pneumothorax, and mediastinal lymphadenopathy (lymph nodes >1 cm in short-axis diameter) were also recorded. The distributions of pulmonary abnormalities were classified as unilateral or bilateral, and peripheral (involving mainly the peripheral one-third of the lung), central (involving mainly the central two-thirds of the lung), or diffuse (involving both peripheral and central regions). Lobar involvement was also recorded (right upper lobe, right middle lobe, right lower lobe, left upper lobe, and/or left lower lobe).

For patients with bacterial pneumonia, only the arched bridge and vacuole signs were recorded. Other CT changes and their distributions were not individually recorded. This component of the analysis was determined based on reports that it is easier to differentiate COVID-19 pneumonia from bacterial pneumonia, whereas it is more difficult to differentiate COVID-19 pneumonia from other types of viral pneumonia.[6,25,26] This manuscript was written in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies.

### Statistical analysis

Imaging findings were compared using the Chi squared test or Fisher's exact test, as appropriate, followed by Bonferroni correction. Comparisons of disease stage, severity, and clinical course among patients with COVID-19 who had the arched bridge and/or vacuole signs were performed using the non-parametric Mann-Whitney *U* test. P values <0.05 were considered indicative of statistical significance. For the arched bridge and vacuole signs, the sensitivity, specificity, positive predictive value, and negative predictive value were calculated, along with the respective 95% confidence intervals. All analyses were conducted using SPSS software (Windows version 25.0; IBM Corp, Armonk [NY], United States).

## Results

### Patients

Among 76 patients with bacterial pneumonia who were admitted for treatment during the study period, five patients with pre-existing lung parenchymal disease were excluded from the analysis: organising pneumonia (n=2), non-specific interstitial pneumonia (n=1), and idiopathic interstitial pneumonia of uncertain subtype (n=2). No patients with COVID-19 required exclusion because of concomitant viral or bacterial infections. The final study population comprised 187 patients: 66 patients with COVID-19 pneumonia, 50 patients with influenza pneumonia, and 71 patients with bacterial pneumonia. The following organisms were detected in patients with bacterial pneumonia: *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Enterococcus* spp., *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Stenotrophomonas* spp., *Serratia* spp., *Acinetobacter* spp., and *Moraxella catarrhalis*. Demographic and clinical characteristics of the study population are shown in Table 1. Compared with patients in the influenza pneumonia and bacterial pneumonia groups, patients with COVID-19 pneumonia tended to be younger and healthier.

### Arched bridge and vacuole signs

The arched bridge and vacuole signs were present

TABLE 1. Comparison of demographic characteristics among patients with pneumonia in Hong Kong*

| Characteristics | COVID-19 pneumonia (n=66) | Influenza pneumonia (n=50) | Bacterial pneumonia (n=71) |
|---|---|---|---|
| Gender | | | |
| Male | 39 (59.1%) | 20 (40.0%) | 52 (73.2%) |
| Female | 27 (40.9%) | 30 (60.0%) | 19 (26.8%) |
| Age, y | 48 ± 16.6 | 61 ± 14.1 | 63 ± 15.8 |
| <20 | 3 (4.5%) | 0 | 0 |
| 20-39 | 21 (31.8%) | 6 (12.0%) | 5 (7.0%) |
| 40-59 | 20 (30.3%) | 16 (32.0%) | 24 (33.8%) |
| ≥60 | 22 (33.3%) | 28 (56.0%) | 42 (59.2%) |
| Co-morbidities | | | |
| Cardiovascular disease | 9 (13.6%) | 22 (44.0%) | 26 (36.6%) |
| Hypertension | 11 (16.7%) | 22 (44.0%) | 30 (42.3%) |
| Diabetes | 9 (13.6%) | 11 (22.0%) | 15 (21.1%) |
| Chronic liver disease | 4 (6.1%) | 12 (24.0%) | 12 (16.9%) |
| Chronic kidney disease | 3 (4.5%) | 17 (34.0%) | 12 (16.9%) |
| Epidemiological contact with COVID-19 | | | |
| Travel history | 50 (75.8%) | | |
| COVID-19 close contact | 22 (33.3%) | | |

Abbreviation: COVID-19 = coronavirus disease 2019

* Data are shown as No. (%) or mean ± standard deviation

in 42 (63.6%) and 14 (21.2%) of 66 patients with COVID-19 pneumonia, respectively (Table 2). The arched bridge sign was commonly in a subpleural location, and there was a smooth arched margin outlining the underside of the GGO or consolidation in all cases (Fig a and b). The vacuole sign was present with GGOs or sites of consolidation in various locations (Fig c and d). The arched bridge sign was much more common in patients with COVID-19 pneumonia than in patients with influenza pneumonia (63.6% vs 8.0%) or bacterial pneumonia (63.6% vs 5.6%, P<0.001). Similarly, the vacuole sign was much more common in patients with COVID-19 pneumonia than in patients with influenza pneumonia (21.2% vs 2.0%, P=0.005) or bacterial pneumonia (21.2% vs 1.4%, P<0.001).

The arched bridge and vacuole signs occurred together in 11 (16.7%) of 66 patients with COVID-19 pneumonia, but they did not occur together in any patients with influenza pneumonia or bacterial pneumonia. Additionally, a review of the five excluded patients with bacterial pneumonia and concurrent pre-existing lung parenchymal disease revealed that none of those patients exhibited the arched bridge sign or the vacuole sign.

In this study, the arched bridge and vacuole signs exhibited high specificities (93.4% and 98.4%, respectively) in terms of identifying COVID-19 pneumonia (Table 3), with moderate or low sensitivities (63.6% and 21.2%, respectively). They also exhibited high positive predictive values (84.0% and 87.5%, respectively) and high or moderate negative predictive values (82.5% and 69.6%, respectively).

The relationships of the arched bridge and vacuole signs with disease course are shown in Table 4. Computed tomography was mainly performed during admission, at a mean of 5.3 days after admission, suggesting these two signs generally appeared at an early stage. Comparisons of patients with COVID-19 pneumonia who had and did not have these two signs revealed that the arched bridge sign was associated with more extensive lung involvement (diseased lobes: 4.0 [present] vs 2.4 [absent], P<0.001). This trend was not evident for the vacuole sign (diseased lobes: 3.8 [present] vs 3.3 [absent]). There was no significant difference in the duration of total hospitalisation between patients with COVID-19 who had and did not have these two signs, suggesting they were not associated with a better or worse prognosis if appropriate treatment was administered.

### Other computed tomography findings

Table 5 shows the comparison of other CT findings between COVID-19 pneumonia and influenza pneumonia. No significant differences were observed in the incidences of GGOs, consolidation, reticular opacities, or crazy paving between patients with COVID-19 and patients with influenza pneumonia (all P>0.05). Air bronchograms (P=0.003), nodules (P=0.009), cavitation (P=0.004), bronchiectasis (P<0.001), pleural effusion (P<0.001), pericardial effusion (P=0.032), and mediastinal lymphadenopathy (P<0.001) were significantly more common in patients with influenza pneumonia.

Abnormalities were more commonly bilateral in patients with COVID-19 pneumonia (77.3%) and patients with influenza pneumonia (96%). The distribution was more likely to be peripheral in patients with COVID-19 pneumonia (51.5% vs 2.0%, P<0.001), and was more likely to be diffuse in patients with influenza pneumonia (98% vs 48.5%, P<0.001). The right upper lobe (P<0.001), right middle lobe (P<0.001), and left upper lobe (P<0.001) were less commonly involved in patients with COVID-19 pneumonia than in patients with influenza pneumonia.

## Discussion

### Arched bridge and vacuole signs

This study evaluated the incidences and diagnostic values of the arched bridge and vacuole signs among patients with COVID-19 pneumonia in a Hong Kong Chinese population. Since the initial description of Wu et al[20] in a series of 11 patients with COVID-19,

TABLE 2. Comparison of patterns of lung sparing morphology among patients with pneumonia in Hong Kong*

| Characteristics | COVID-19 pneumonia (n=66) | Influenza pneumonia (n=50) | Bacterial pneumonia (n=71) | P value |
|---|---|---|---|---|
| Arched bridge sign | 42 (63.6) | 4 (8.0) | 4 (5.6) | <0.001‡ § |
| Vacuole sign | 14 (21.2) | 1 (2.0) | 1 (1.4) | 0.005‡, <0.001§ |
| Arched bridge and vacuole signs† | 11 (16.7) | 0 | 0 | |

Abbreviation: COVID-19 = coronavirus disease 2019

* Data are shown as No. (%), unless otherwise specified

† Both signs present in combination

‡ COVID-19 vs influenza pneumonia

§ COVID-19 vs bacterial pneumonia

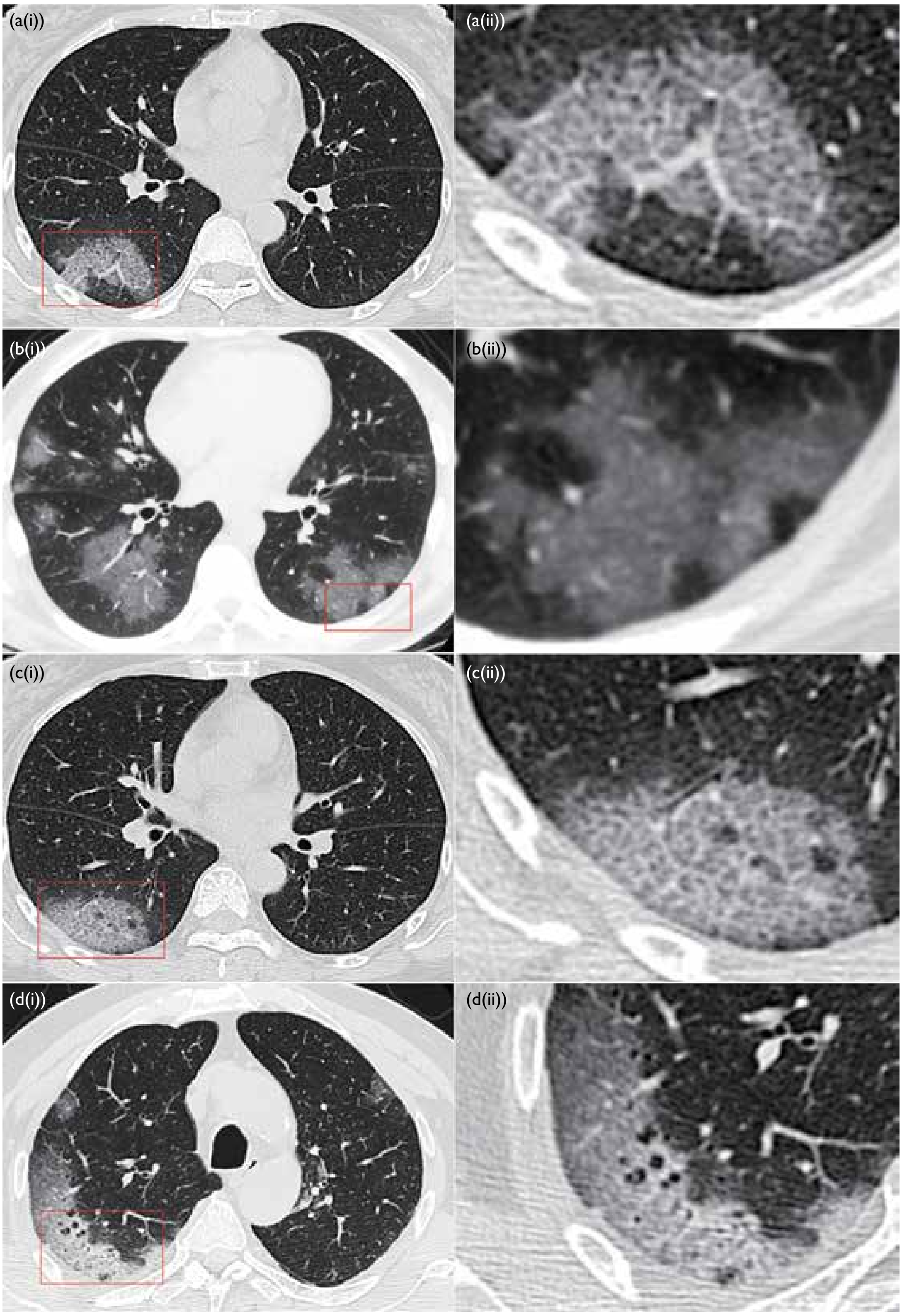


FIG. (a) The arched bridge sign. Axial computed tomography (CT) image (i) and magnified view of boxed area (ii) in a 56-year-old woman with coronavirus disease 2019 (COVID-19) pneumonia showing an arched ground-glass opacity (GGO) with a sharp underside outlining a semicircular region of spared lung. The typical subpleural location for the sign is evident. (b) Axial CT image (i) and magnified view of boxed area (ii) in a 35-year-old man with COVID-19 pneumonia showing a subpleural GGO with a sharp arched margin outlining two adjacent regions of spared lung, demonstrating a double arched bridge appearance. Other GGOs are also evident involving both central and peripheral lung parenchyma. (c) Vacuole sign. Axial CT image (i) and magnified view of boxed area (ii) in a 55-year-old woman with COVID-19 pneumonia showing a subpleural GGO with a few very small vacuole-like regions of sparing in the affected region. (d) Axial CT image (i) and magnified view of boxed area (ii) in a 56-year-old man with COVID-19 pneumonia showing a subpleural GGO with multiple very small vacuoles

TABLE 3. Diagnostic performances of the arched bridge and vacuole signs for coronavirus disease 2019 pneumonia*

| Characteristics | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|---|---|---|---|---|
| Arched bridge sign | 63.6% (50.9-75.1%) | 93.4% (87.4-97.1%) | 84.0% (72.4-91.3%) | 82.5% (77.3-86.7%) |
| Vacuole sign | 21.2% (12.1-33.0%) | 98.4% (94.2-99.8%) | 87.5% (62.1-96.8%) | 69.6% (66.8-72.2%) |
| Arched bridge and vacuole signs† | 16.7% (8.6-27.9%) | 100.0% (97.0-100.0%) | 100.0% (74.1-100.0%) | 68.7% (66.4-71.0%) |

* Data are shown as percentage (95% confidence interval)
† Both signs present in combination

TABLE 4. Comparison of disease stage, severity, and clinical course among patients with coronavirus disease 2019 pneumonia according to arched bridge sign and vacuole sign statuses*

| | Disease stage (time from symptom onset), d† | Disease stage (time from admission), d† | Disease severity: lobes‡ | Duration of total hospitalisation, d |
|---|---|---|---|---|
| Arched bridge sign | | | | |
| Present (n=42) | 8.8 ± 8.1 (0-48)§ | 5.6 ± 6.3 (1-38) | 4.0 ± 1.3 (1-5) | 26.9 ± 13.5 (4-70) |
| Absent (n=24) | 9.6 ± 3.7 (0-16)§ | 4.9 ± 2.3 (1-9) | 2.4 ± 1.6 (1-5) | 33.5 ± 15.1 (8-75) |
| P value | 0.772 | 0.308 | <0.001 | 0.968 |
| Vacuole sign | | | | |
| Present (n=14) | 7.9 ± 3.8 (3-15)§ | 5.2 ± 2.4 (2-9) | 3.8 ± 1.4 (1-5) | 29.4 ± 13.2 (7-50) |
| Absent (n=52) | 9.2 ± 7.3 (0-48)§ | 5.4 ± 5.6 (1-38) | 3.3 ± 1.7 (1-5) | 29.2 ± 14.4 (4-75) |
| P value | 0.904 | 0.395 | 0.741 | 0.960 |

* Data are shown as mean ± standard deviation (range), unless otherwise specified
† Days from symptom onset or admission at time of computed tomography
‡ Total No. of lobes involved
§ Asymptomatic patients were excluded from analysis in the following categories: arched bridge sign present (n=1), arched bridge sign absent (n=3), vacuole sign present (n=1), and vacuole sign absent (n=3)

our study is the first to validate the arched bridge sign in patients with COVID-19. To our knowledge, this is also the first study to evaluate the vacuole sign in non–COVID-19–related pneumonia. The arched bridge sign was significantly more common in COVID-19 pneumonia than in influenza pneumonia or bacterial pneumonia. Additionally, the incidences of the vacuole sign and both signs observed in combination were higher (or tended to be higher) in patients with COVID-19 pneumonia than in patients with influenza pneumonia or bacterial pneumonia. Our results imply that these two signs generally appeared at an early stage; the arched bridge sign is more likely to be observed in patients with more severe lung pathology. These results suggest that the arched bridge and vacuole signs can be used in CT-based identification of COVID-19 pneumonia, as well as efforts to differentiate COVID-19 pneumonia from other types of infection-related pneumonia. Currently, chest CT is not recommended for the screening or diagnosis of COVID-19 pneumonia when RT-PCR tests are available. In selected cases, CT can be used to monitor clinical progress and identify complications of the disease. In some scenarios, CT can be a useful alternative investigation method for COVID-19 diagnosis or triage, such as healthcare settings with restricted access to RT-PCR tests.[27,28] When these two signs are observed on CTs performed for COVID-19 pneumonia or other indications during the COVID-19 pandemic, physicians should carefully consider a diagnosis of COVID-19 pneumonia. However, our findings indicated there was no significant difference in the duration of total hospitalisation between patients with COVID-19 pneumonia who had and did not have these two signs, suggesting that they are not indicative of a better or worse prognosis if appropriate treatments are administered.

The underlying pathophysiological mechanisms behind these signs remain unclear. However, the morphological appearances of the arched bridge and vacuole signs may indicate different pathophysiological mechanisms of lung sparing that occur during infection-related pneumonia. Histopathological examinations of

TABLE 5. Comparison of other computed tomography findings between patients with coronavirus disease 2019 pneumonia and patients with influenza pneumonia*

| Characteristics | COVID-19 pneumonia (n=66) | Influenza pneumonia (n=50) | P value |
|---|---|---|---|
| GGOs | 56 (84.8) | 37 (74.0) | 0.147 |
| Consolidation | 53 (80.3) | 43 (86.0) | 0.421 |
| GGOs + consolidation | 33 (50.0) | 31 (62.0) | 0.198 |
| Reticular opacities | 32 (48.5) | 27 (54.0) | 0.556 |
| Crazy paving | 11 (16.7) | 11 (22.0) | 0.468 |
| Air bronchograms | 31 (47.0) | 37 (74.0) | 0.003 |
| Nodules | 10 (15.2) | 18 (36.0) | 0.009 |
| Cavitation | 1 (1.5) | 8 (16.0) | 0.004 |
| Bronchiectasis | 2 (3.0) | 14 (28.0) | <0.001 |
| Pleural retraction or thickening | 19 (28.8) | 16 (32.0) | 0.709 |
| Pleural effusion | 2 (3.0) | 25 (50.0) | <0.001 |
| Pericardial effusion | 0 | 4 (8.0) | 0.032 |
| Pneumothorax | 0 | 0 | - |
| Mediastinal lymphadenopathy | 0 | 21 (42.0) | <0.001 |
| Location | | | |
| Unilateral | 15 (22.7) | 2 (4.0) | 0.005 |
| Bilateral | 51 (77.3) | 48 (96.0) | 0.005 |
| Distribution | | | |
| Peripheral | 34 (51.5) | 1 (2.0) | <0.001 |
| Central | 0 | 0 | - |
| Diffuse | 32 (48.5) | 49 (98.0) | <0.001 |
| Lobar involvement | | | |
| Right upper lobe | 36 (54.5) | 42 (84.0) | <0.001 |
| Right middle lobe | 31 (47.0) | 43 (86.0) | <0.001 |
| Right lower lobe | 58 (87.9) | 45 (90.0) | 0.720 |
| Left upper lobe | 44 (66.7) | 47 (94.0) | <0.001 |
| Left lower lobe | 57 (86.4) | 45 (90.0) | 0.552 |

Abbreviations: COVID-19 = coronavirus disease 2019; GGOs = ground-glass opacities

* Data are shown as No. (%), unless otherwise specified

lung biopsy tissues from patients with COVID-19 pneumonia have provided evidence of variations in diffuse alveolar damage.[29,30] The curved concave margin in the arched bridge sign may be the result of secondary pulmonary lobule sparing, with the interlobular septum of the secondary pulmonary nodule forming some resistance to the spread of infection among lobules.[20] In contrast, the vacuole sign (ie, a very small focal lucent area) may reflect a spared alveolar cluster or dilated alveolar sac within an area of otherwise involved lung.[21,23] Zhang et al[23] reported that the vacuole sign was often present in patients with advanced COVID-19 pneumonia, where alveolar sac dilation could result from damage to the alveolar wall.

The incidence of the arched bridge sign in patients with COVID-19 (63.6%) was similar to the incidence reported by Wu et al[20] (72.7%). The incidence of the vacuole sign (21.2%) in patients with COVID-19 pneumonia is also within the range reported in prior studies describing this sign (17-66%).[21-24] Notably, three additional case series have revealed spared airspaces in patients with COVID-19 pneumonia, comprising 'round cystic changes'[31], 'cystic air spaces'[32] and 'cavity signs',[33] with prevalences of 10 to 30%; these phenomena may include the vacuole sign. However, these case series did not include formal definitions of the findings. The differences in definitions of the vacuole sign (and phenomena that include the sign) may also explain the disparate prevalences (17%-66%, as noted above) reported in the literature.

The arched bridge and vacuole signs differentiated COVID-19 pneumonia from influenza pneumonia and bacterial pneumonia with high specificities and high positive predictive values, suggesting that these signs can help to provide a specific imaging diagnosis of COVID-19 pneumonia. When encountering inconclusive CT features of COVID-19 pneumonia, these signs can be identified with minimal additional effort; their presence may be sufficient to increase suspicion or add to the evidence confirming a diagnosis of COVID-19 pneumonia. The respective sensitivities of the arched bridge and vacuole signs were moderate (63.6%) and low (21.2%); the arched bridge sign may be more useful in this context. Our findings suggest that the combined presence of the arched bridge and vacuole signs strongly supports a diagnosis of COVID-19 pneumonia.

Consistent with previous studies, the presence of nodules, cavitations, bronchiectasis, pleural effusion, pericardial effusion, and/or mediastinal lymphadenopathy was uncommon in patients with COVID-19 pneumonia; these features were more common in patients with influenza pneumonia.[12,16-18,34,35] Our results indicated that COVID-19-related abnormalities on CT were generally bilateral and peripheral, compatible with the findings in prior studies.[12-14]

## Limitations

This study had several limitations. First, it used a retrospective design, and patients were imaged in a cross-sectional manner at various time intervals after symptom onset. Computed tomography was not regularly performed, which hindered the monitoring or analysis of imaging signs over time. Second, CT was not routinely performed for patients with influenza pneumonia or bacterial pneumonia; it was performed based on clinical judgement, generally because of patient deterioration or poor response to treatment. We did not assess differences in the clinical features of patients with influenza pneumonia and patients with bacterial pneumonia between patients who did and did not undergo CT. Third, we attempted to implement diversity in our analysis of COVID-19 pneumonia by comparisons with influenza pneumonia and bacterial pneumonia, whereas prior studies have generally been limited to comparisons of COVID-19 pneumonia with influenza pneumonia. However, we did not examine other types of viral pneumonia; we also did not conduct subgroup analysis according to influenza subtype. Additionally, we did not systematically compare the prognoses of patients with non–COVID-19 pneumonia who had and did not have the arched bridge or vacuole signs. This comparison was hindered by the sample size, because these two signs were very uncommon in patients with non–COVID-19 pneumonia. However, additional analysis did not reveal a clear pattern whereby these two signs would be predictive for clinical prognosis in patients with non–COVID-19 pneumonia. Finally, the sample size in this study was moderate. Although the prevalences of the arched bridge and vacuole signs in our patients with COVID-19 pneumonia were consistent with findings in the literature, their diagnostic specificities should be validated in other types of pneumonia. Despite these limitations, the high diagnostic specificities of these CT signs provide insights that will be useful in future studies. Additional work is needed regarding the relationships of these CT signs with clinical status, and our findings require validation in larger and more diverse patient populations.

# Conclusion

In conclusion, two morphological patterns of lung sparing, namely the arched bridge and vacuole signs, are much more common in patients with COVID-19 pneumonia; they have the potential to differentiate COVID-19 pneumonia from influenza pneumonia and bacterial pneumonia. In this study, these signs had high specificities and positive predictive values for COVID-19 pneumonia. The identification of these signs in clinical practice may be useful for increasing suspicion or providing confirmatory evidence to support a diagnosis of COVID-19 pneumonia.

### Author contributions

Concept and design: TY So, SCH Yu, JYX Wang.
Acquisition of data: All authors.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: TY So, S Yu, JYX Wang.
Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

### Conflicts of interest

The authors have no conflicts of interest to disclose.

### Acknowledgement

The authors thank Ms Apurva Sawhney, Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, for assistance with data collection.

### Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

### Ethics approval

This study was approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (REC Ref. No.: 2020.232), which waived the requirement for informed consent due to the retrospective nature of the study. The study was conducted in compliance with the established ethical standards and principles of the Declaration of Helsinki.

### References

1. Kim H. Outbreak of novel coronavirus (COVID-19): what is the role of radiologists? Eur Radiol 2020;30:3266-7.
2. Yang W, Sirajuddin A, Zhang X, et al. The role of imaging in 2019 novel coronavirus pneumonia (COVID-19). Eur Radiol 2020;30:4874-82.
3. Pan F, Ye T, Sun P, et al. Time course of lung changes at chest CT during recovery from coronavirus disease 2019 (COVID-19). Radiology 2020;295:715-21.
4. Wang Y, Dong C, Hu Y, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. Radiology. 2020;296:E55-64.
5. Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral pneumonia. Radiographics 2018;38:719-39.
6. Sun Z, Zhang N, Li Y, Xu X. A systematic review of chest imaging findings in COVID-19. Quant Imaging Med Surg 2020;10:1058-79.
7. Marcos MA, Esperatti M, Torres A. Viral pneumonia. Curr Opin Infect Dis 2009;2:143-7.
8. Apisarnthanarak A, Mundy LM. Etiology of community-acquired pneumonia. Clin Chest Med 2005;26:47-55.
9. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA 2020;323:1824-36.
10. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. JAMA 2020;324:782-93.
11. Zayet S, Kadiane-Oussou NJ, Lepiller Q, et al. Clinical features of COVID-19 and influenza: a comparative study on Nord Franche-Comte cluster. Microbes Infect 2020;22:481-8.
12. Lin L, Fu G, Chen S, et al. CT manifestations of coronavirus disease (COVID-19) pneumonia and influenza virus pneumonia: a comparative study. AJR Am J Roentgenol 2021;216:71-9.
13. Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology 2020;295:202-7.

14. Song F, Shi N, Shan F, et al. Emerging 2019 novel coronavirus (2019-nCoV) pneumonia. Radiology 2020;295:210-7.
15. Wang H, Wei R, Rao G, Zhu J, Song B. Characteristic CT findings distinguishing 2019 novel coronavirus disease (COVID-19) from influenza pneumonia. Eur Radiol 2020;30:4910-7.
16. Bai HX, Hsieh B, Xiong Z, et al. Performance of radiologists in differentiating COVID-19 from non–COVID-19 viral pneumonia on chest CT. Radiology 2020;296:E45-54.
17. Yin Z, Kang Z, Yang D, Ding S, Luo H, Xiao E. A comparison of clinical and chest CT findings in patients with influenza A (H1N1) virus infection and coronavirus disease (COVID-19). AJR Am J Roentgenol 2020;215:1065-71.
18. Liu M, Zeng W, Wen Y, Zheng Y, Lv F, Xiao K. COVID-19 pneumonia: CT findings of 122 patients and differentiation from influenza pneumonia. Eur Radiol 2020;30:5463-9.
19. Tanaka N, Matsumoto T, Kuramitsu T, et al. High resolution CT findings in community-acquired pneumonia. J Comput Assist Tomogr 1996;20:600-8.
20. Wu R, Guan W, Gao Z, et al. The arch bridge sign: a newly described CT feature of the coronavirus disease-19 (COVID-19) pneumonia. Quant Imaging Med Surg 2020;10:1551-8.
21. Zhou S, Wang Y, Zhu T, Xia L. CT features of coronavirus disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. AJR Am J Roentgenol 2020;214:1287-94.
22. Sabri YY, Nassef AA, Ibrahim IM, Abd El Mageed MR, Khairy MA. CT chest for COVID-19, a multicenter study—experience with 220 Egyptian patients. Egypt J Radiol Nucl Med 2020;51:144.
23. Zhang L, Kong X, Li X, et al. CT imaging features of 34 patients infected with COVID-19. Clin Imaging 2020;68:226-31.
24. Zhou S, Zhu T, Wang Y, Xia L. Imaging features and evolution on CT in 100 COVID-19 pneumonia patients in Wuhan, China. Eur Radiol 2020;30:5446-54.
25. Elmokadem AH, Bayoumi D, Abo-Hedibah SA, El-Morsy A. Diagnostic performance of chest CT in differentiating COVID-19 from other causes of ground-glass opacities. Egypt J Radiol Nucl Med 2021;52:12.
26. Zheng F, Li L, Zhang X, et al. Accurately discriminating COVID-19 from viral and bacterial pneumonia according to CT images via deep learning. Interdiscip Sci 2021;13:273-85.
27. 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 - Secondary Publication. J Thorac Imaging 2020;35:219-27.
28. Dennie C, Hague C, Lim RS, et al. Canadian Society of Thoracic Radiology/Canadian Association of Radiologists consensus statement regarding chest imaging in suspected and confirmed COVID-19. Can Assoc Radiol J 2020;71:470-81.
29. Bradley BT, Maioli H, Johnston R, et al. Histopathology and ultrastructural findings of fatal COVID-19 infections in Washington State: a case series. Lancet 2020;396:320-32.
30. Zhang H, Zhou P, Wei Y, et al. Histopathologic changes and SARS-CoV-2 immunostaining in the lung of a patient with COVID-19. Ann Intern Med 2020;172:629-32.
31. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020;20:425-34.
32. Rodrigues RS, Barreto MM, Werberich GM, Marchiori E. Cystic airspaces associated with COVID-19 pneumonia. Lung India 2020;37:551-3.
33. Kong W, Agarwal PP. Chest imaging appearance of COVID-19 infection. Radiol Cardiothorac Imaging 2020;2:e200028.
34. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020;215:87-93.
35. Xu Z, Pan A, Zhou H. Rare CT feature in a COVID-19 patient: cavitation. Diagn Interv Radiol 2020;26:380-1.