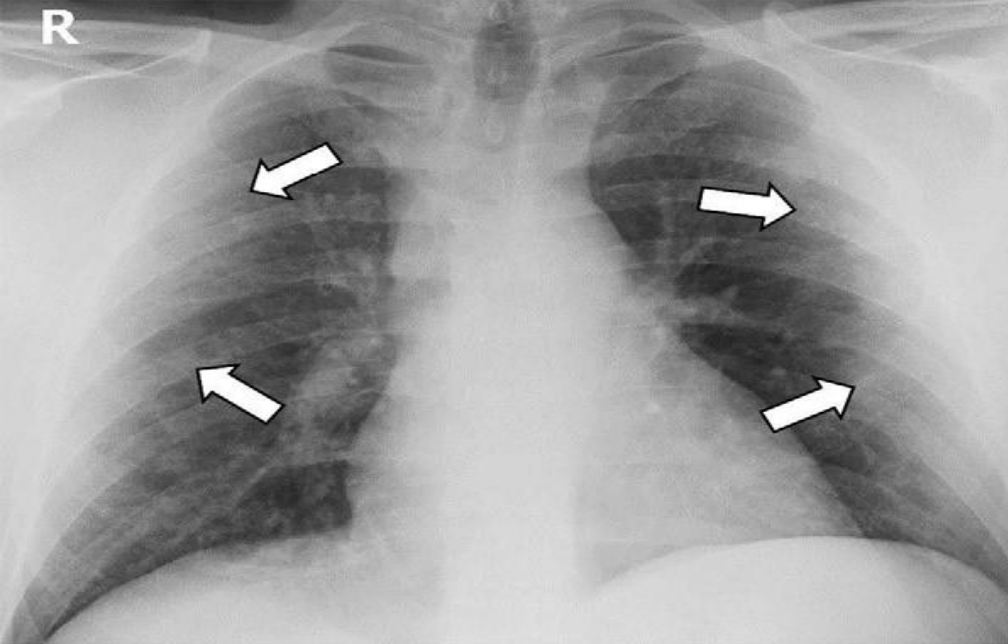


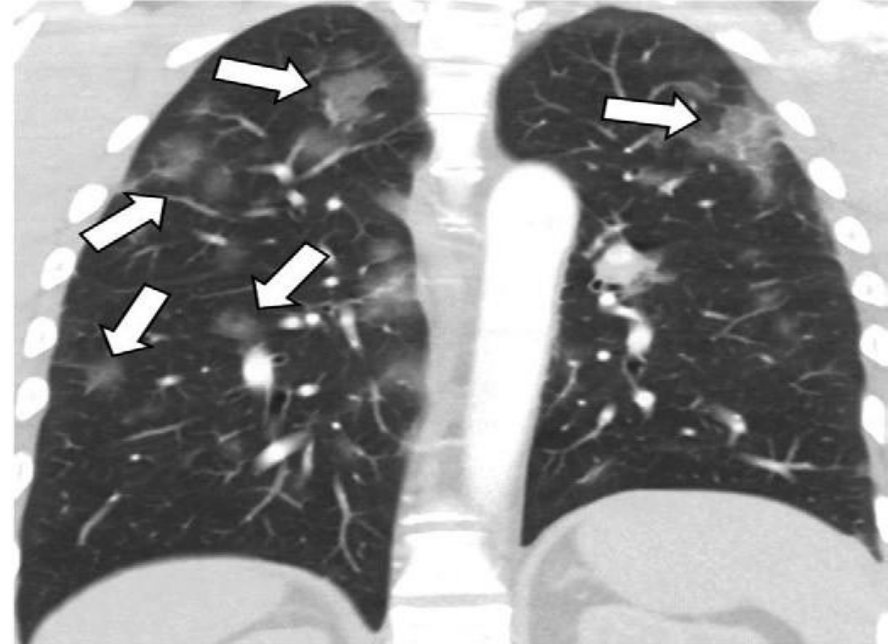
COVID-19 Imaging: What We Know Now and What Remains Unknown

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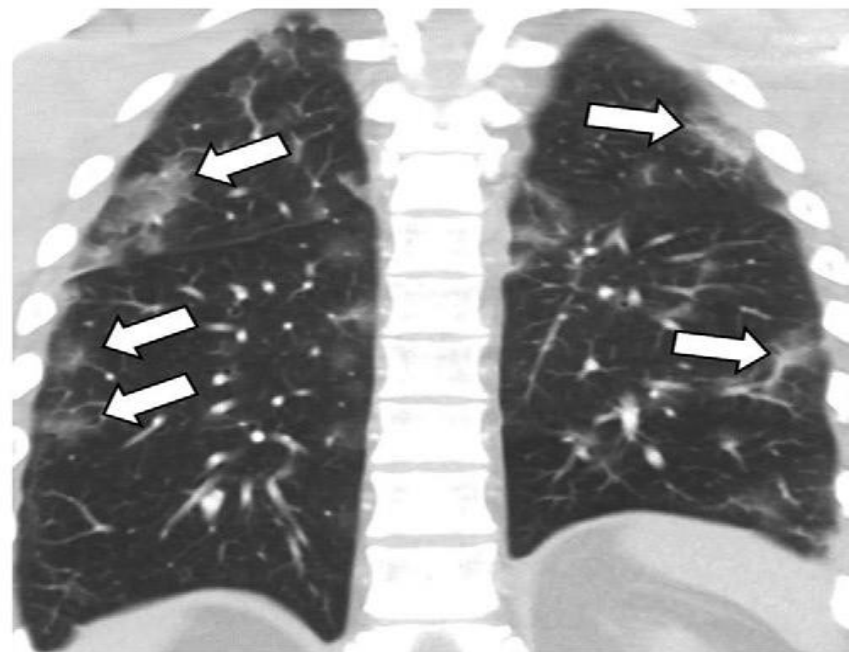


a.



b.

Images in a 37-year-old woman with COVID-19 presenting with fever, cough, nausea, and diarrhea for 1 week. **(a) Posteroanterior** chest radiograph shows mild, ill-defined pulmonary opacities in periphery of lungs bilaterally (arrows). **(b, c) Coronal contrast-enhanced CT images** of chest show corresponding peripheral ground-glass opacities bilaterally (arrows), some with rounded morphologic presentation.



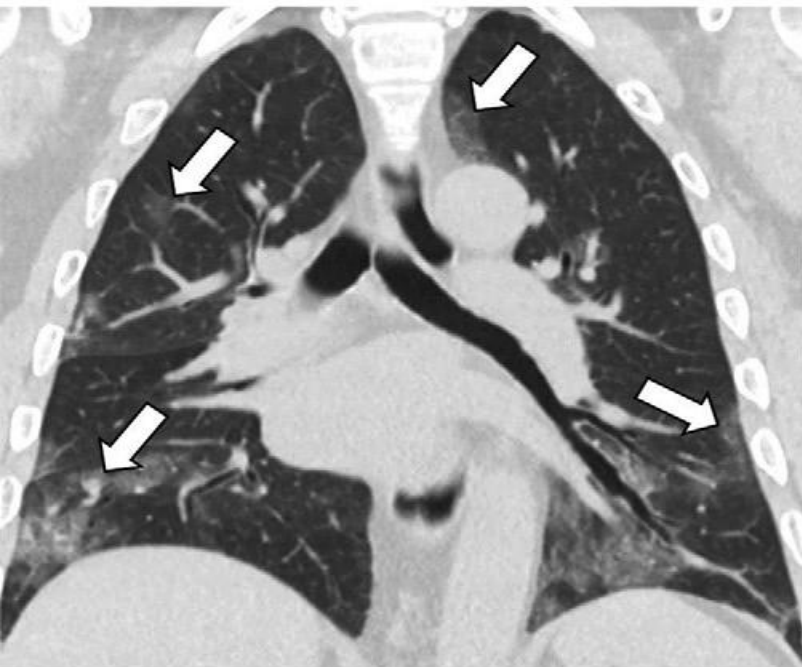
c.



a.

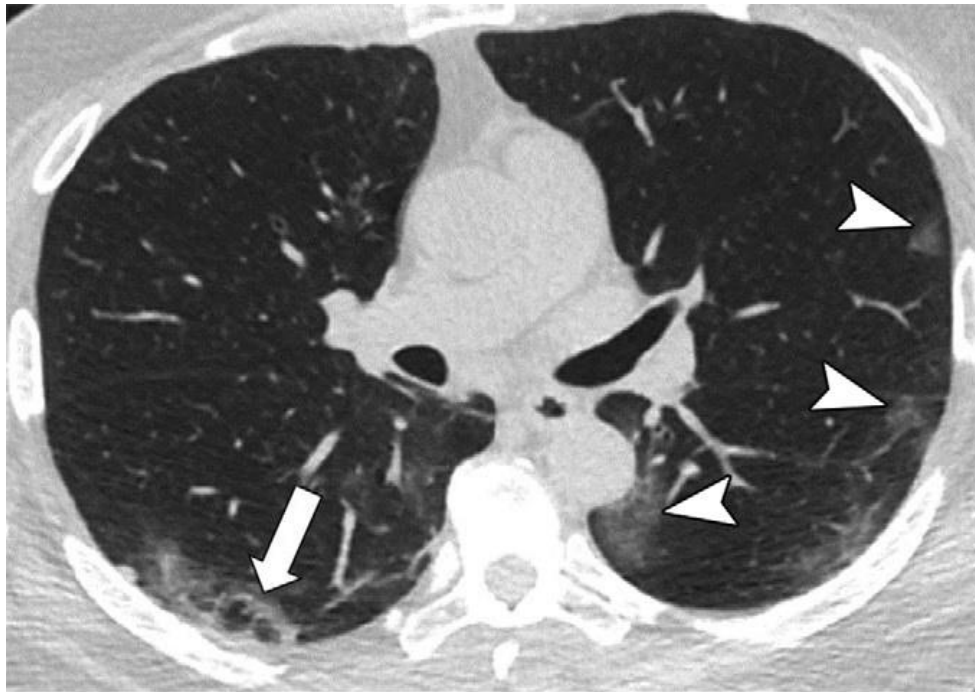


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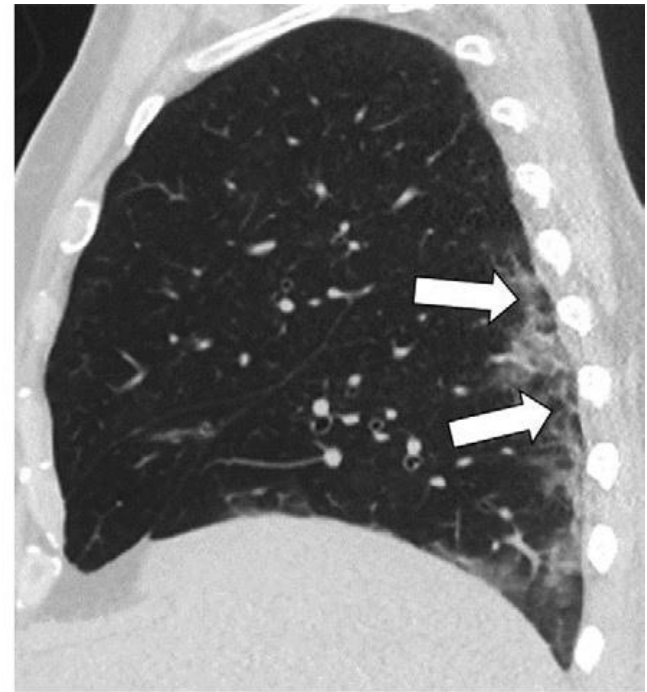


c.

Images in a 77-year-old man with COVID-19 presenting with 5 days of fever and cough. **(a, b) Axial and (c) coronal unenhanced thin-section chest CT** images show bilateral ground-glass opacities (arrows) in predominately peripheral distribution, and many have rounded morphologic presentation.

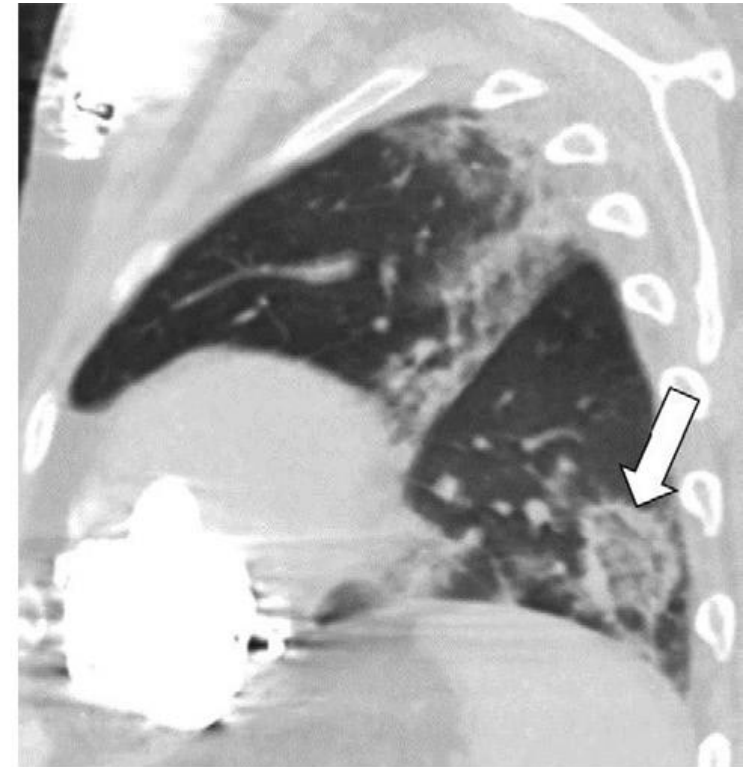
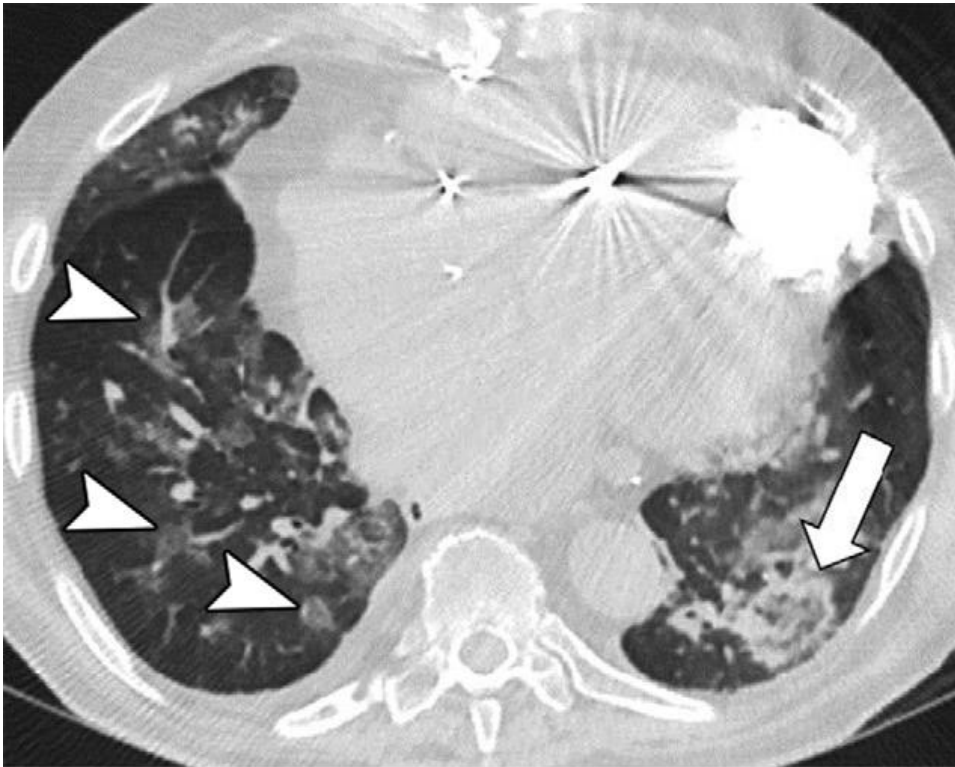


a.



b.

Images in a 57-year-old man with COVID-19 presenting with 4 days of cough. **(a) Axial and (b) sagittal unenhanced thinsection** chest CT images show bilateral ground-glass opacities in peripheral distribution in left lung, some with rounded morphologic presentation (arrowheads). There are also arcadelike opacities in subpleural right lower lobe (arrows), indicative of perilobular pattern of disease.



a.

b.

Images in a 72-year-old man with COVID-19 and a history of heart failure presenting with 10 days of cough. **(a) Axial and (b) sagittal unenhanced thin-section chest CT images show peribronchial ground-glass opacities (arrowheads), as well as ground-glass opacity in left lower lobe with ring of denser consolidation (reverse halo sign) (arrow).**

Table 1: Summary of Radiological Society of North America Expert Consensus Reporting System for COVID-19

Category and Description

Typical appearance

Peripheral, bilateral GGO with or without consolidation or visible intralobular lines (crazy paving)

Multifocal GGO of rounded morphologic presentation with or without consolidation or visible intralobular lines (crazy paving)

Reverse halo sign or other findings of organizing pneumonia (seen later in the disease)

Indeterminate appearance

Absence of typical features AND presence of:

Multifocal, diffuse, perihilar, or unilateral GGOs with or without consolidation that lack a specific distribution; that are nonrounded or nonperipheral and lack a specific distribution; or that are nonrounded or nonperipheral

Few very small GGOs with a nonrounded and nonperipheral distribution

Atypical appearance

Absence of typical or indeterminate features AND presence of:

Isolated lobar or segmental consolidation without GGO

Discrete small nodules (centrilobular, “tree-in-bud”)

Lung cavitation

Smooth interlobular septal thickening with pleural effusion

Negative for pneumonia

No CT features to suggest pneumonia

Note.—Summary is compiled from reference 12. GGO = ground-glass opacity.

Table 2: Summary of CO-RADS

Category and Description

6: Proven

RT-PCR test is positive for SARS-CoV-2

5: Very high suspicion: typical for COVID-19

GGO, with or without consolidations, in lung regions close to visceral pleural surfaces, including the fissures (subpleural sparing is allowed) and multifocal bilateral distribution AND at least one of the following:

Ground-glass regions

Nonsharp demarcation, (half) rounded shape

Sharp demarcation, outlining the shape of multiple adjacent secondary pulmonary lobules

Crazy paving

Patterns compatible with organizing pneumonia

Thickened vessels within parenchymal abnormalities found in all confirmatory patterns

4: High suspicion: suspicious for COVID-19

Findings are similar to those for CO-RADS 5 category but

Not in contact with the visceral pleura

Not located strictly unilaterally in a predominant peribronchovascular distribution

Superimposed on severe diffuse preexisting pulmonary abnormalities

3: Equivocal/unsure: features compatible with COVID-19 but also other diseases

Perihilar GGO

Homogeneous extensive GGO with or without sparing of some secondary pulmonary lobules

GGO together with smooth interlobular septal thickening with or without pleural effusion in the absence of other typical CT findings

Small GGOs that are not centrilobular or not located close to the visceral pleura

Patterns of consolidation compatible with organizing pneumonia without other typical findings of COVID-19

2: Low suspicion: typical for other infection but not for COVID-19

CT findings in the lungs typical of infectious origin that are considered incompatible with COVID-19. Examples include the following:

Bronchitis

Infectious bronchiolitis

Bronchopneumonia

Lobar pneumonia

Pulmonary abscess

Features including the following:

Tree-in-bud sign

Centrilobular nodular pattern

Lobar or segmental consolidation

Lung cavitation

1: Very low suspicion

Normal or noninfectious

0: Not interpretable

Image technically insufficient for assigning a score

Note.—Summary is compiled from reference 37. CO-RADS = COVID-19 Reporting and Data System, GGO = ground-glass opacity, RT-PCR = reverse transcriptase–polymerase chain reaction.

Table 3: Summary of British Society of Thoracic Imaging System

Category and Description

Classic COVID-19: 100% confidence

Lower lobe predominant, peripheral predominant, multiple, bilateral foci of GGO, with or without:

Crazy paving

Peripheral consolidation

Air bronchograms

Reverse halo or perilobular pattern

Probable COVID-19: 71%–99% confidence

Lower lobe predominant mix of bronchocentric and peripheral consolidation

Reverse halo or perilobular pattern

GGOs scarce

Indeterminate: <70% confidence for COVID-19

Does not fit into definite, probable, or non-COVID-19

Manifests above patterns, but the clinical context is wrong or suggests an alternative diagnosis

Non-COVID-19: 70% confidence for alternative

Lobar pneumonia

Cavitating infections

Tree-in-bud or centrilobular nodularity

Lymphadenopathy, effusions

Established pulmonary fibrosis

Note.—Summary is compiled from reference 38. GGO = ground-glass opacity.

Table 4: Summary of COVID-RADS

Category and Description

3: High suspicion

Typical findings

Multifocal GGO

GGO with superimposed consolidation

Consolidation predominant pattern (late or complicated)

Linear opacities (late or complicated)

Crazy-paving pattern (late or complicated)

Melted sugar sign (late or remission)

2A: Moderate suspicion

Fairly typical findings

Single GGO (early)

Consolidation without GGO (late or complicated)

Focal pleural thickening associated with GGO or consolidation

Vascular dilation or mural thickening

Air bronchogram

Bronchial wall thickening

White lung stage (late or complicated)

Parenchymal fibrotic bands (late or remission)

2B: Moderate suspicion

Combination of atypical findings with typical or fairly typical findings

1: Low suspicion

Atypical findings:

Pleural effusion

Cavity

Pulmonary nodule(s)

Nodular pattern

Lymphadenopathy

Peribronchovascular distribution

Halo sign

Tree-in-bud sign

Bronchiectasis

Airway secretions

Pulmonary emphysema

Pulmonary fibrosis

Isolated pleural thickening

Pneumothorax

Pericardial effusion

0: Low suspicion

Normal

Note.—Summary is compiled from reference 39. COVID-RADS = COVID-19 Imaging Reporting and Data System, GGO = ground-glass opacity.

Table 5: Summary of COVID-19 Structured Reporting System

Category and Description

Compatible with COVID-19

Bilateral elementary COVID-19 lesions only or predominantly in lower zones (lower zones with or without upper and middle zones)

Bilateral elementary COVID-19 lesions in all zones without predominance

Elementary lesions defined as pure GGO or GGO with consolidation (consolidation may be smaller in the central region of the lesion or may occupy most of the lesion [halo sign]) that has the following characteristics:

Rounded or lobulated or geographic contours (not diffuse)

Discrete or coalescent

Peripheral with or without bronchocentric (not central)

Predominantly posterior localization

Accompanying intralesional intralobular reticulations (crazy paving), bronchial dilation, air bronchogram, vascular enlargement, air bubble, curvilinear irregular thick lines, perilobular sparing, or reverse halo sign

Indeterminate

Bilateral elementary COVID-19 lesions located predominantly in upper or middle zones

Single or multiple elementary COVID-19 lesions in single lower zone unless consolidation is dominant

Unilateral elementary COVID-19 lesions predominantly in lower zone

GGO that does not have the characteristic of an elementary COVID-19 lesion, but does not exactly fit any other diagnosis

Alternative diagnosis

Unilateral elementary COVID-19 lesions located predominantly in upper or middle zones

Absence of typical features of an elementary COVID-19 lesion and presence of:

Opacity that affects a large and continuous area of a lobe (lobar pneumonia) or of one or more secondary lobules of a lung presenting segmental consolidation (bronchopneumonia)

Bronchiolitis (tree-in-bud sign or centrilobular nodularity)

Cavitating infection

Bronchial wall thickening

Lymphadenopathy, pleural effusions

Smooth interlobular septal thickening

Normal

No CT features to suggest pneumonia

Note.—Summary is compiled from reference 40. GGO = ground-glass opacity.

Table 6: Reporting Systems for Chest Radiography

British Society of Thoracic Imaging	U.S. Multicenter
Classic or probable COVID-19	Typical appearance
Lower lobe and peripheral predominant multiple opacities that are bilateral	Multifocal bilateral, peripheral opacities
Indeterminate for COVID-19	Opacities with rounded morphologic presentation
Does not fit classic or non-COVID-19 descriptors	Lower lung-predominant distribution
Non-COVID-19	Indeterminate appearance
Pneumothorax	Absence of typical findings AND
Lobar pneumonia	Unilateral, central, or upper lung-predominant distribution
Pleural effusion	Atypical appearance
Pulmonary edema	Pneumothorax
Other	Pleural effusion
Normal	Pulmonary edema
	Lobar consolidation
	Solitary lung nodule or mass
	Diffuse tiny nodules
	Cavity
	Negative for pneumonia
	No lung opacities

Note.—Summaries are compiled from references 38 and 43 (British Society of Thoracic Imaging) and reference 44 (U.S. multicenter).

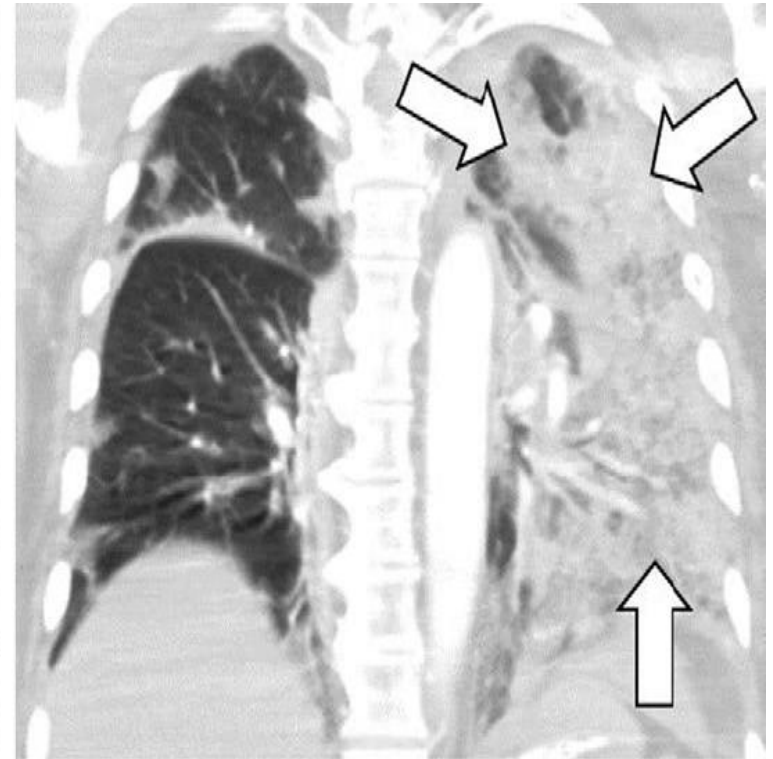
Table 7: Summary of Artificial Intelligence Studies for COVID-19

Study	Journal	Country	Modality	No. of Patients	Purpose	EV	Acc	AUC	PR AUC	Sen	Spec	C Index	F_1 Score
Li et al (58)	<i>Radiology</i>	China	CT	3322	Diagnosis	No	NA	0.96	NA	0.90	0.96	NA	NA
Bai et al (59)	<i>Radiology</i>	U.S.	CT	1186	Diagnosis	Yes	0.87	0.90	0.87	0.89	0.86	NA	NA
Mei et al (60)	<i>Nature Medicine</i>	U.S.	CT	905	Diagnosis	No	NA	0.92	NA	0.84	0.83	NA	NA
Zhang et al (61)	<i>Cell</i>	China	CT	3777	Diagnosis, severity assessment	Yes	0.91	0.97	NA	0.93	0.86	NA	NA
Murphy et al (62)	<i>Radiology</i>	Nl	Radiography	1549	Diagnosis	Yes	NA	0.81	NA	0.85	0.61	NA	NA
Lessmann et al (63)	<i>Radiology</i>	Nl	CT	843	Severity assessment	Yes	NA	0.88	NA	0.82	0.81	NA	NA
Liu et al (64)	<i>Theranostics</i>	China	CT	134	Prognosis	No	NA	0.93	NA	NA	NA	0.88	NA
Wang et al (65)	<i>European Respiratory Journal</i>	China	CT	5372	Diagnosis, prognosis	Yes	0.78	0.87	NA	0.80	0.77	NA	0.77
Harmon et al (66)	<i>Nature Communications</i>	U.S.	CT	2617	Diagnosis	Yes	0.90	0.94	NA	0.85	0.92	NA	NA
Ning et al (67)	<i>Nature Biomedical Engineering</i>	China	CT	1521	Prognosis	Yes	0.76	0.81	NA	0.76	0.76	NA	NA
Jin et al (68)	<i>Nature Communications</i>	China	CT	9025	Diagnosis	Yes	NA	0.93	NA	0.94	0.66	NA	NA
Zhang et al (69)	<i>Radiology</i>	U.S.	Radiography	5208	Diagnosis	No	NA	0.92	NA	0.88	0.79	NA	NA

Note.—Deep learning technique was used for all studies. Acc = accuracy, AUC = area under the curve, EV = external validation, NA = not applicable, Nl = the Netherlands, PR = precision-recall, Sen = sensitivity, Spec = specificity, U.S. = United States.

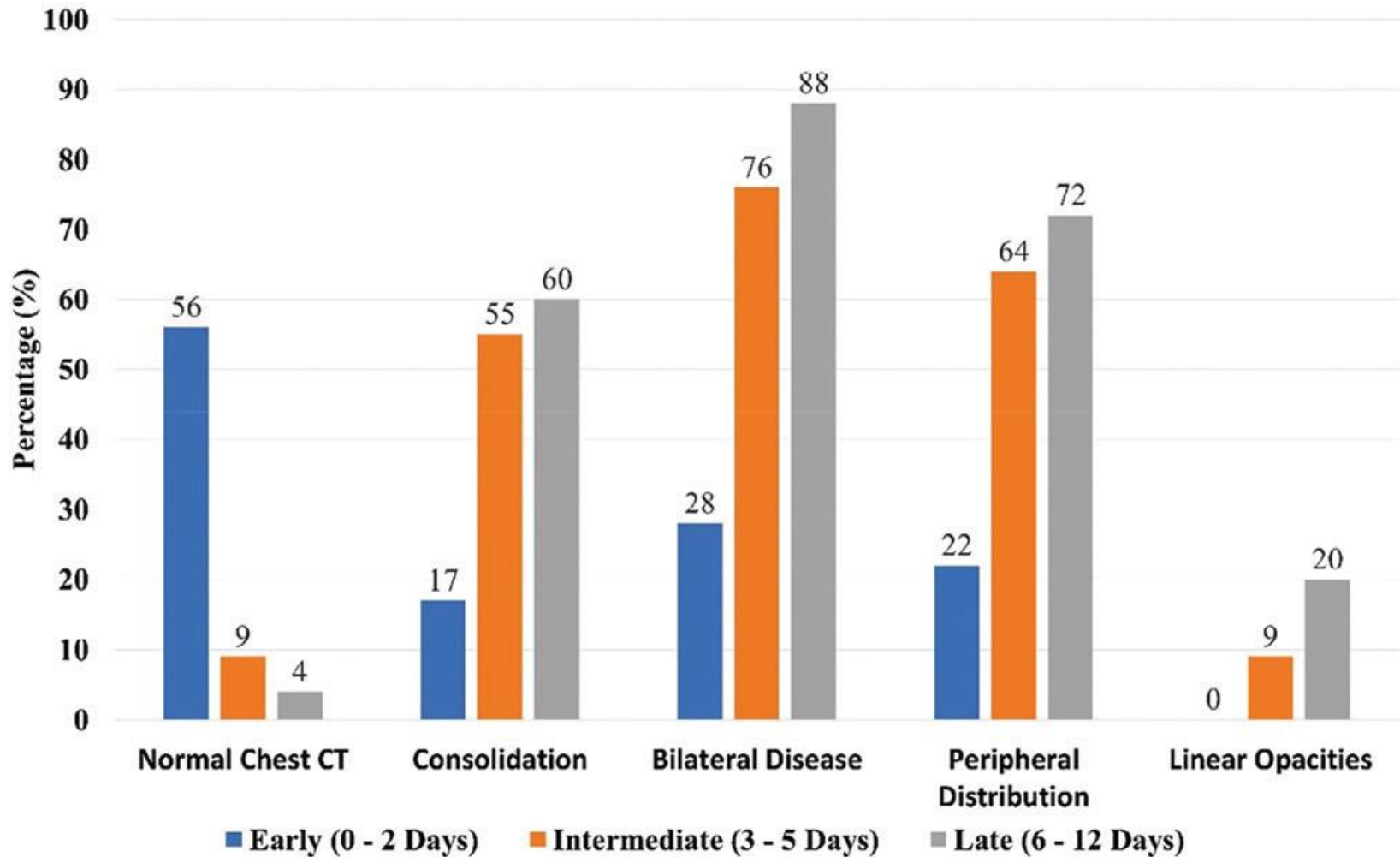


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b.

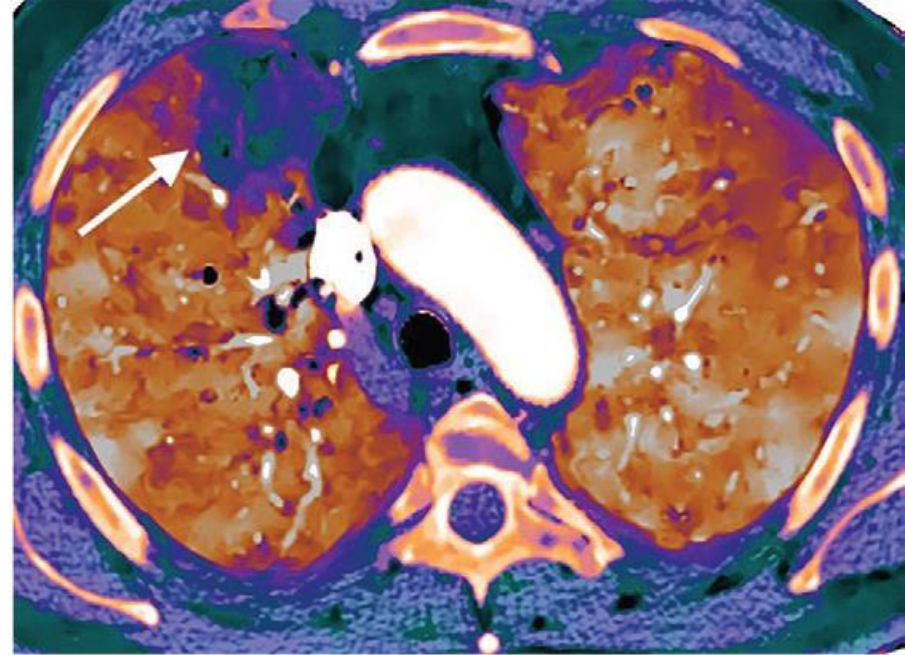
Images in a 74-year-old man with COVID-19 presenting with 7 days of cough. **(a) Axial and (b) coronal contrast-enhanced thin-section** chest CT images show diffuse ground-glass opacity and consolidation in left lung (arrows). These findings would be classified as indeterminate as per the Radiological Society of North America, British Society of Thoracic Imaging, and COVID-19 structured reporting assessment systems; these findings would be classified as equivocal/unsure as per the COVID-19 Reporting and Data System.



Graph shows frequency of selected chest CT findings as function of time course from symptom onset. Adapted, with permission, from reference 14.

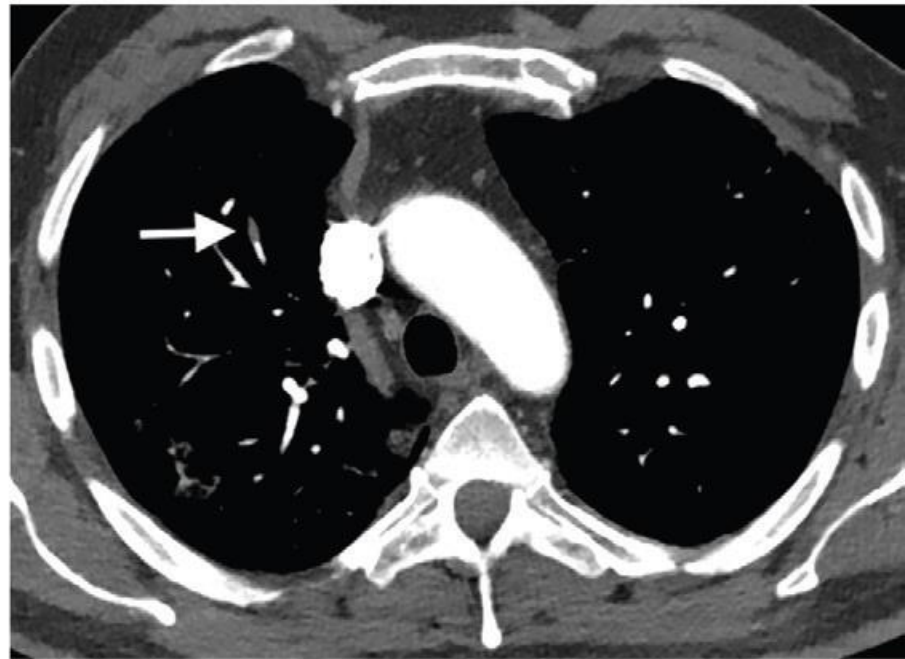


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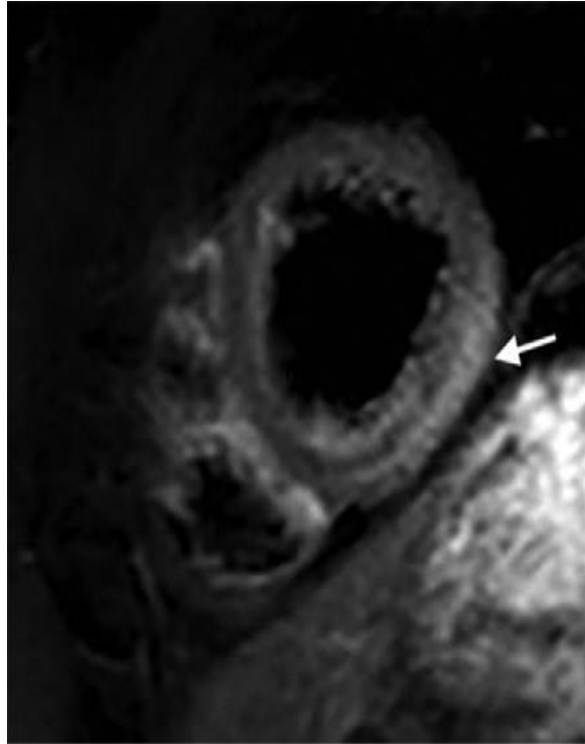


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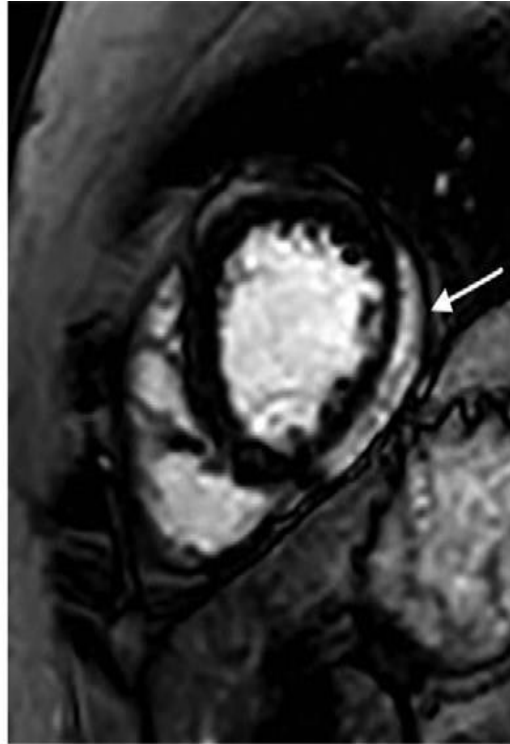
Images in a 59-year-old man with COVID-19, diabetes, hypertension, and coronary arterial disease presenting with shortness of breath and fever. **(a) Contrast-enhanced CT angiographic image (lung window settings)** shows bilateral peripheral ground-glass opacity. Dilated vessel (arrow) is present in anterior right upper lobe within region of lung opacity. **(b) Spectral contrast-enhanced CT pulmonary blood volume map** shows subsegmental perfusion defect (arrow) in anterior right upper lobe, in territory of dilated vessel. **(c) Contrast-enhanced CT angiographic image (vascular window settings)** shows isolated subsegmental filling defect (arrow) corresponding to dilated vessel in subsegmental anterior right upper lobe pulmonary artery, which is consistent with acute pulmonary embolism or in situ thrombus.



c.



a.

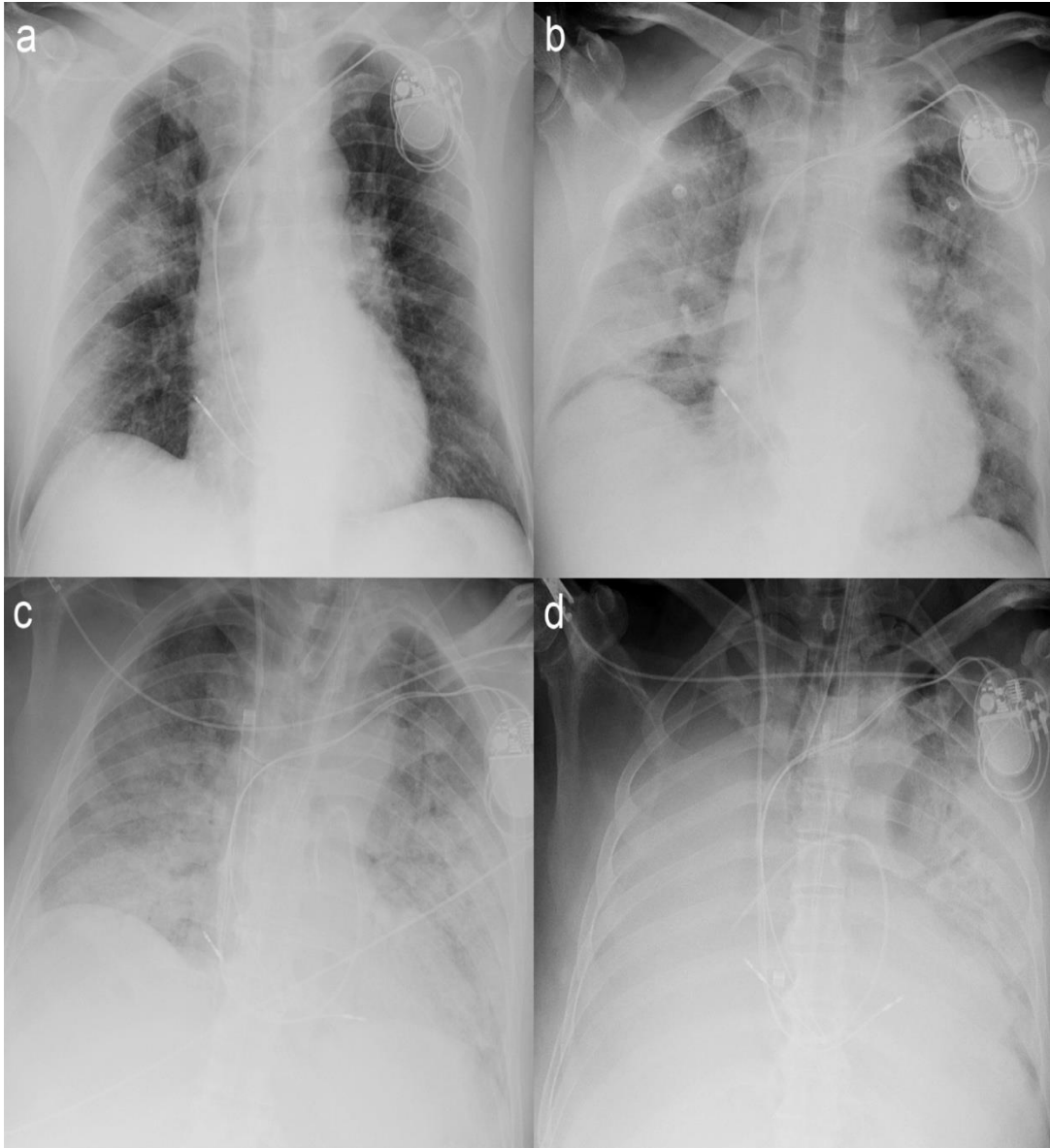


b.



c.

Images in a 22-year-old man with COVID-19, shortness of breath, and chest pain. Cardiac MRI demonstrates mildly reduced left ventricular systolic function with ejection fraction of 47%. **(a) T2 short-axis image through apical segments demonstrates subepicardial edema (high signal, arrow) along lateral wall. (b, c) There is corresponding subepicardial lateral wall late gadolinium enhancement on short-axis (arrow in b) and four-chamber (arrows in c) images.**



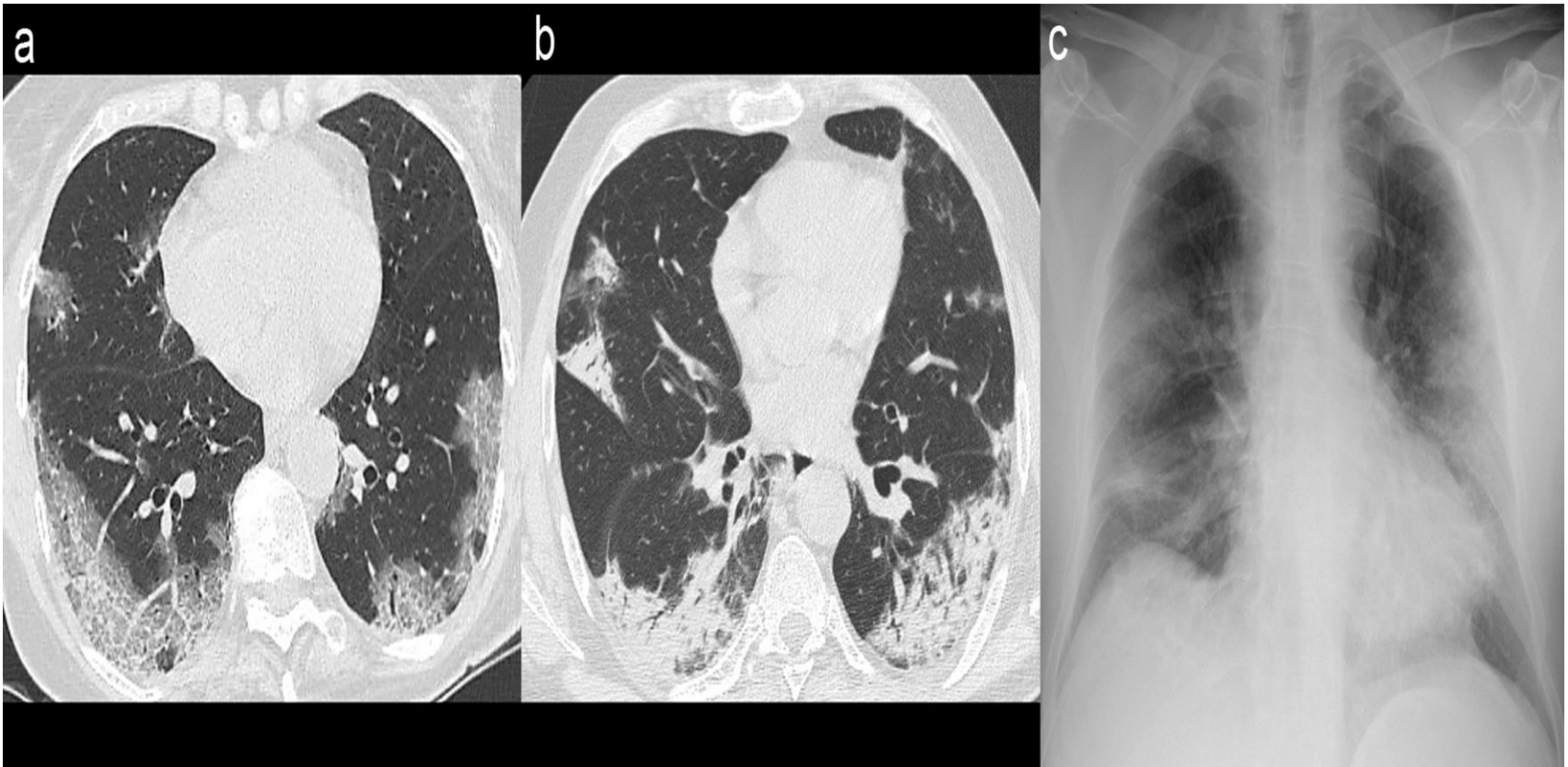
Worsening evolution of COVID-19 pneumonia in a 63- year-old male with known cardiac disease (note the presence of a pacemaker).

The first antero-posterior (AP) chest X-ray (CXR) (a) shows hazy opacities with a mid-basal and peripheral predominance on the right lung, without pleural effusion.

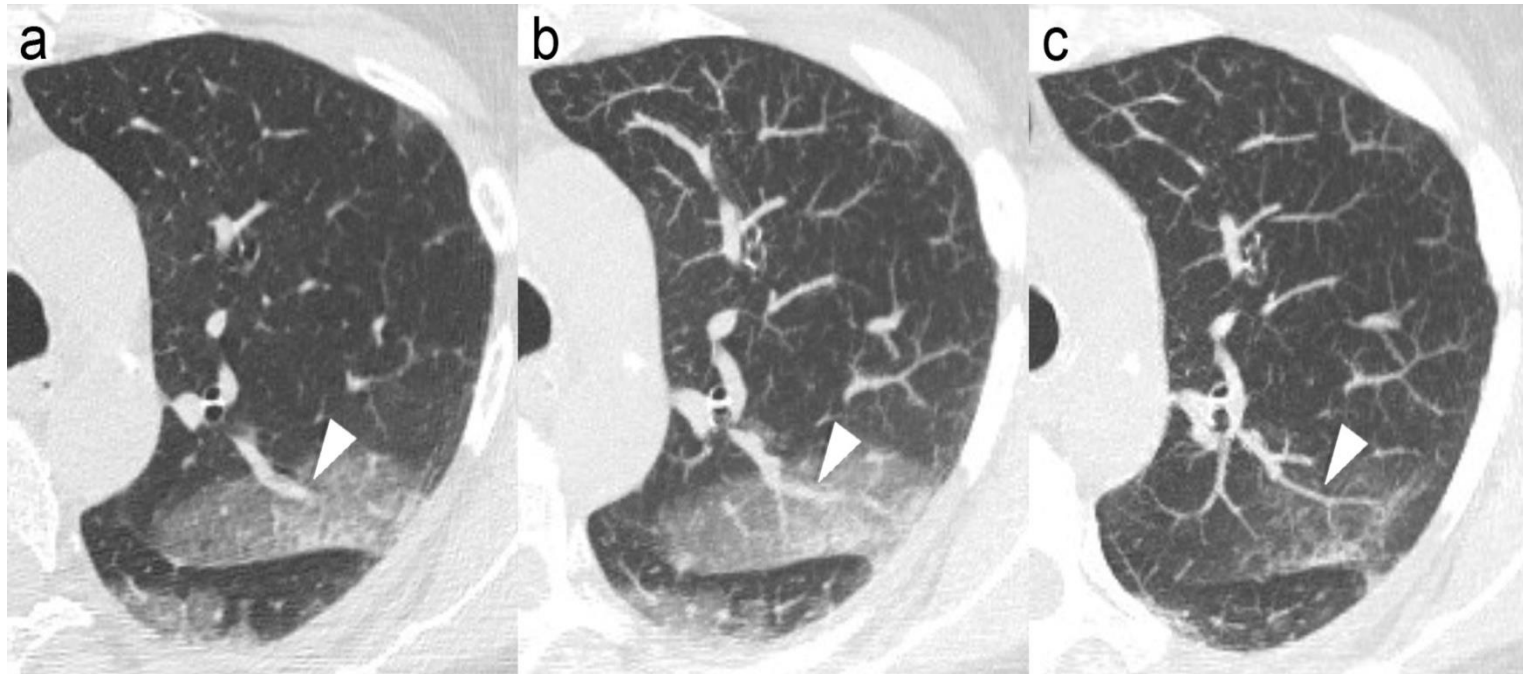
Two days later, the AP CXR (b) depicts confluent and bilateral alveolar opacities with air bronchogram and quite diffuse distribution.

CXR performed 9 days later in ICU (c) shows a further increase of bilateral alveolar opacities, especially in the mid-basal lungs.

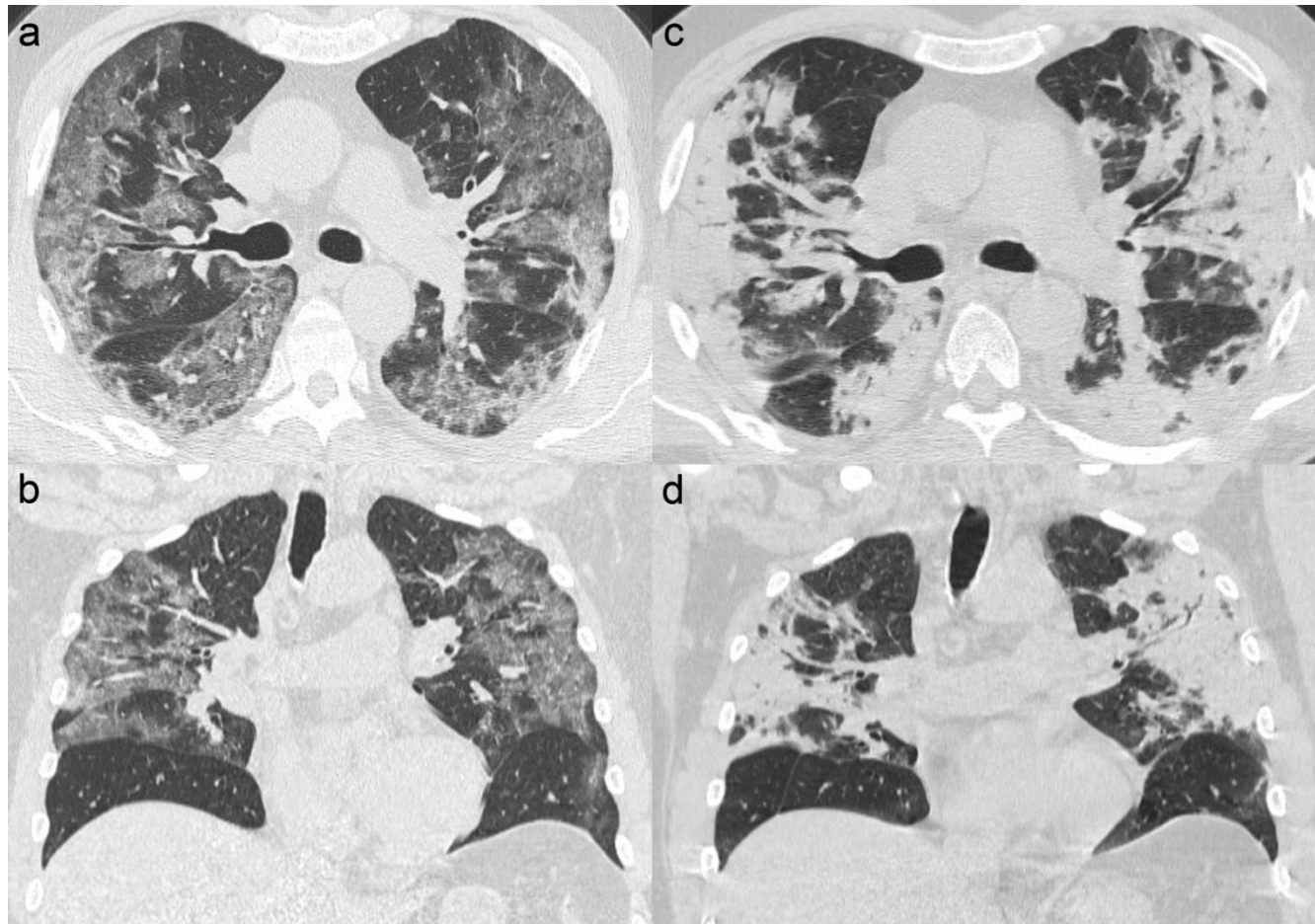
In the last CXR (d), a further radiographic worsening was evident, with development of bilateral "whited lung". The patient deceased two days later due to ARDS.



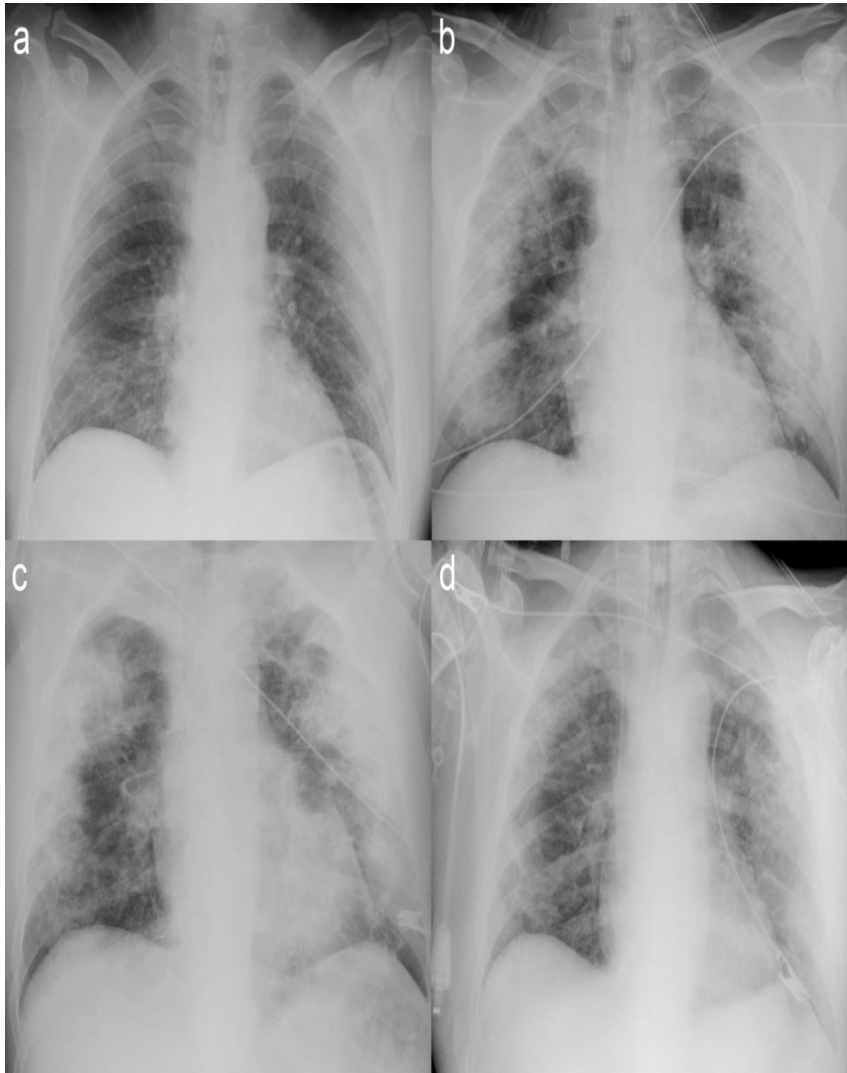
Common findings of COVID-19 pneumonia in two different patients. In the first patient, the axial HRCT image (a) shows bilateral, dorsal, subpleural areas of *crazy paving*. In the second patient, the axial HRCT image (b) demonstrates patchy bilateral consolidations with subpleural and dorsal distribution, and lower lobes volume loss. Chest X-ray (CXR) (c) of the same case as in b nicely depicts the bilateral peripheral mid-basal distribution of the opacities.



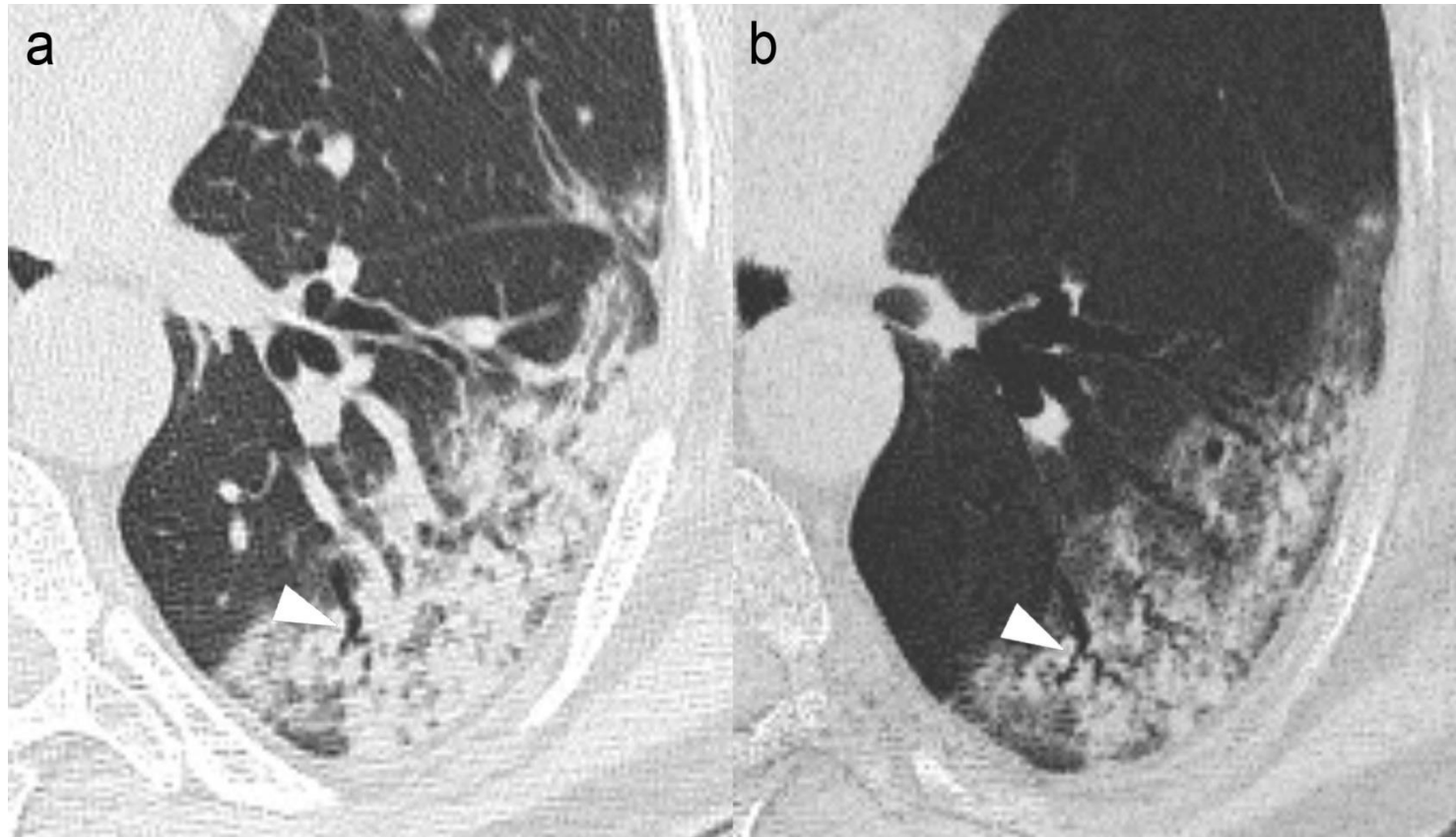
Axial HRCT image (a) and maximum intensity projection (MIP) (b) in the *early phase* of COVID-19 pneumonia show enlargement (>3 mm) of a segmental pulmonary artery within the GG area in the apico- posterior segment of the left upper lobe (arrowhead in a and in b). Axial HRCT MIP image (c), performed 10 days later, shows a normal caliber of the same vessel at the same anatomical level (arrowhead in c). Note the consensual shrinkage of the focal GG area



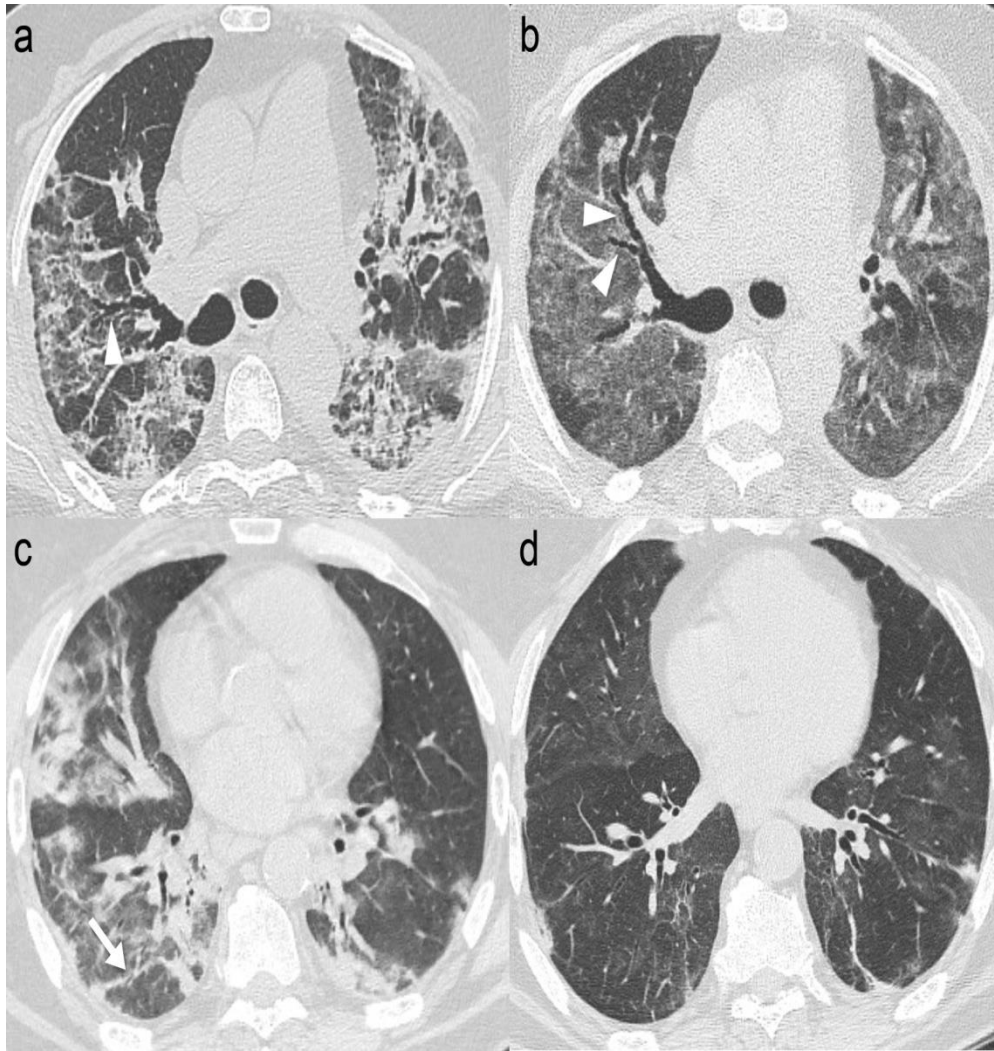
Temporal evolution of COVID-19 pneumonia on HRCT. Axial (a) and coronal (b) HRCT images show bilateral GG opacities with a predominant peripheral distribution, located in the mid-upper lungs (*early phase* disease). Axial (c) and coronal (d) HRCT performed 9 days later demonstrate the typical evolution in the *progressive phase*, with extensive consolidations in the same areas previously involved by GG opacities. Note the overall mild lung volume reduction in d.



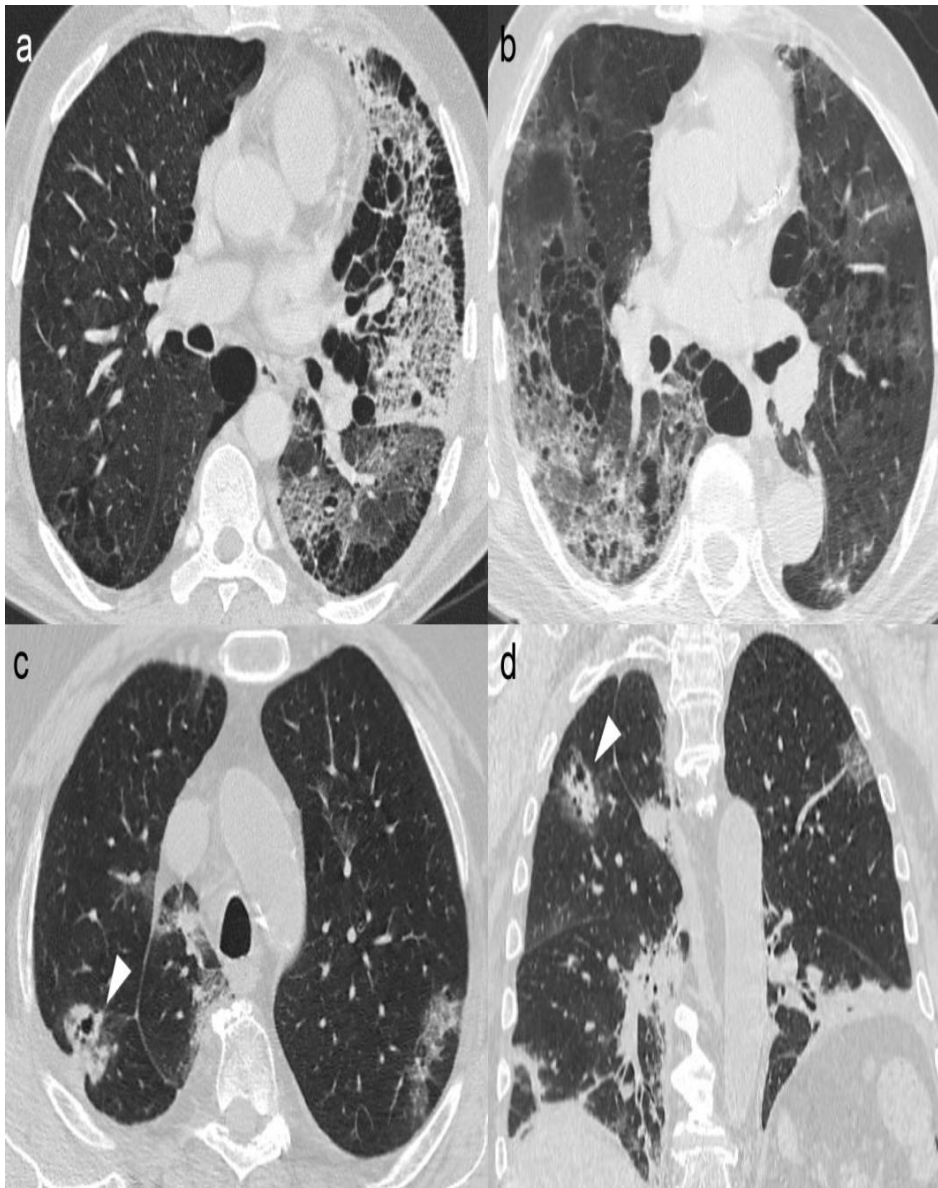
Temporal evolution of COVID-19 pneumonia on chest X-ray (CXR) in the same patient as in Fig. 4. The first AP CXR (a) performed to admission in the emergency room shows ill-defined hazy opacities in the peripheral regions of both lung, especially in the left mid-zone and in the right lung base. Images (b) and (c), performed 4 and 7 days later, respectively, demonstrate a progressive increase of the opacities in terms of extension and density with progressive lung volume reduction in c. Patient experienced a clinical and radiological improvement two weeks later with reduction of lung opacities (d).



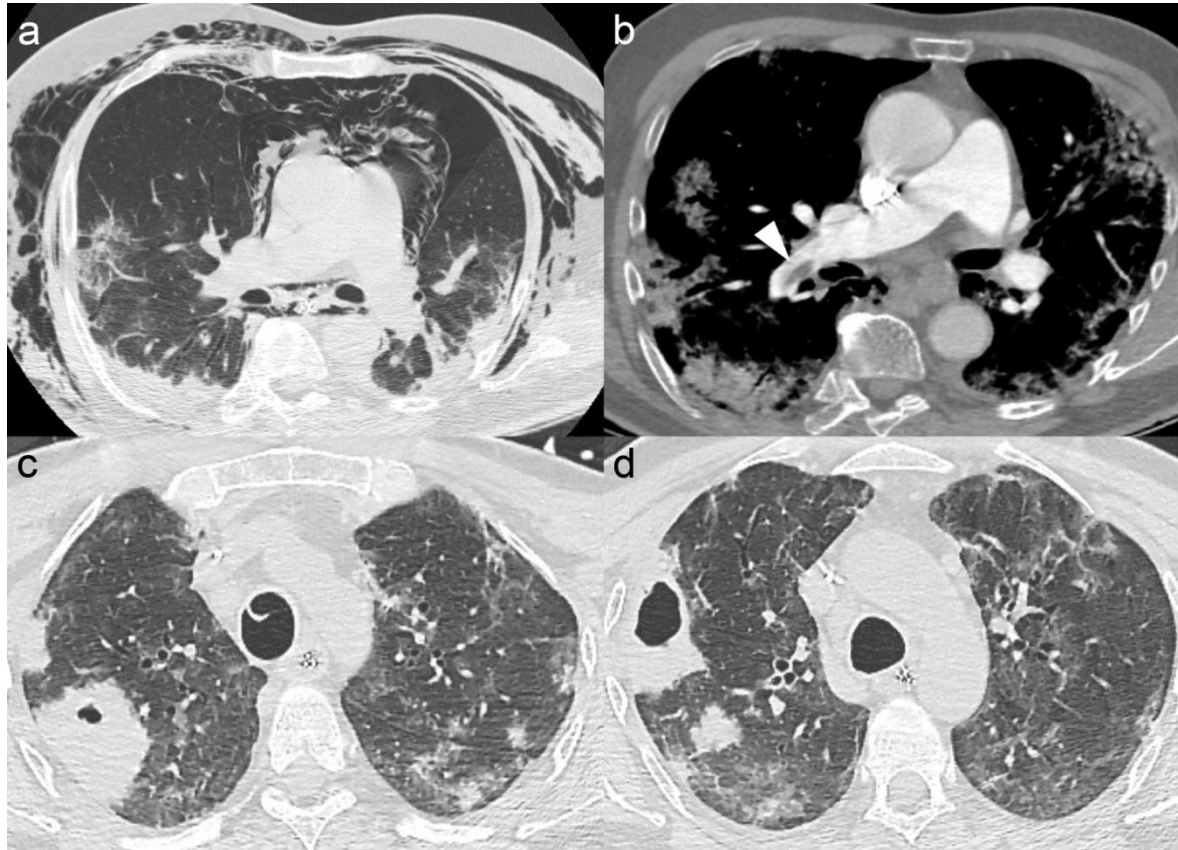
Axial HRCT image (a) depicts traction bronchiectasis (arrowheads) within the peripheral area of consolidation in the left lower lobe, in a case of COVID-19 pneumonia in the *progressive phase*. The axial HRCT mIP (minimum intensity projection) image (b) enhances the visibility of traction bronchiectasis and bronchiolectasis within the same area (arrowhead).



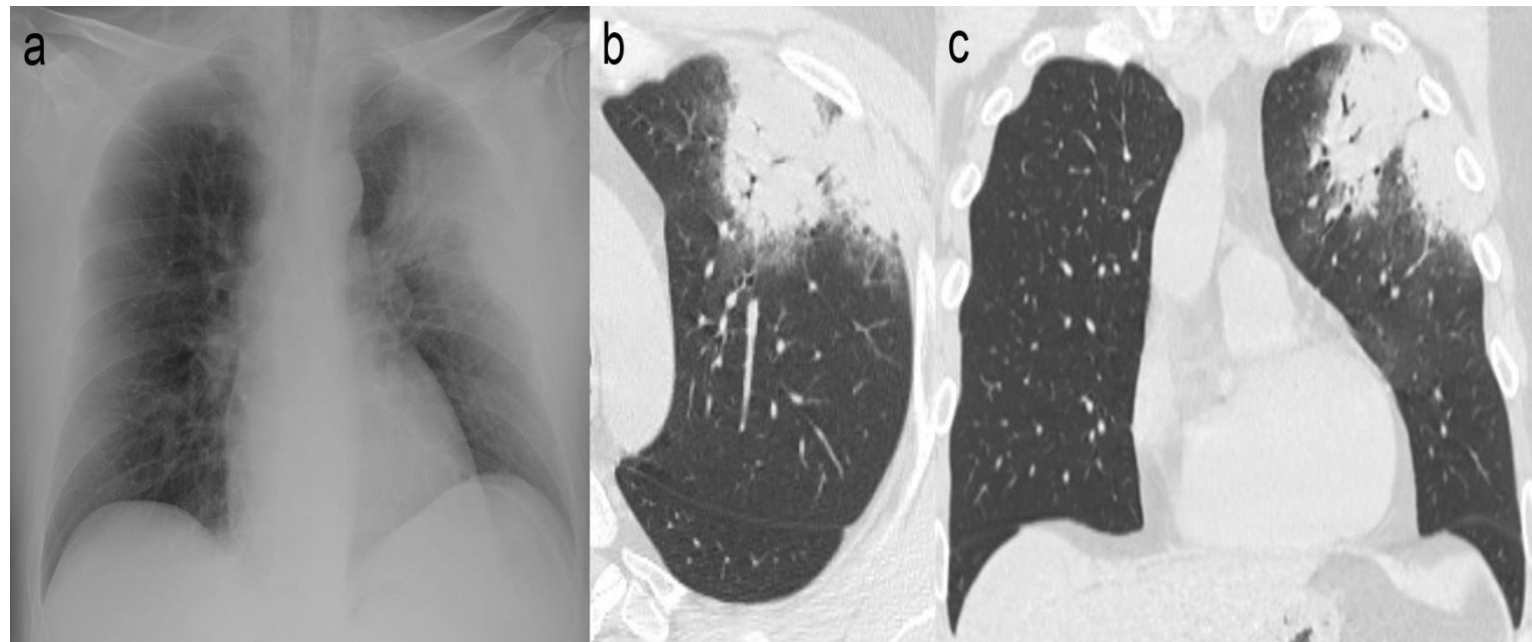
Progressive (a, c) and absorption stages (b, d) on HRCT of two different patients with COVID-19 pneumonia. In the first patient, the axial HRCT image in the progressive stage (a) demonstrates areas of consolidation with mild parenchymal retraction and traction bronchiectasis (arrowhead). The axial HRCT performed 12 days later (b) shows bilateral GG opacities which are more extended than the previously detected consolidation (*"tinted" sign*). Traction bronchiectasis within the GG opacities are still present (arrowheads). These findings should always be interpreted, looking at the previous scans, as normal evolution towards the resolution of abnormalities and not as persistent or worsening disease after a complete clinical recovery. In the second patient, the axial HRCT image in the progressive stage (c) depicts consolidations, mild GG opacities and perilobular opacities (arrow), more extensive in the right lung. The axial HRCT performed 16 days later (d) demonstrates almost complete resolution of the findings, with some residual faint ill-defined GG areas and linear opacities.



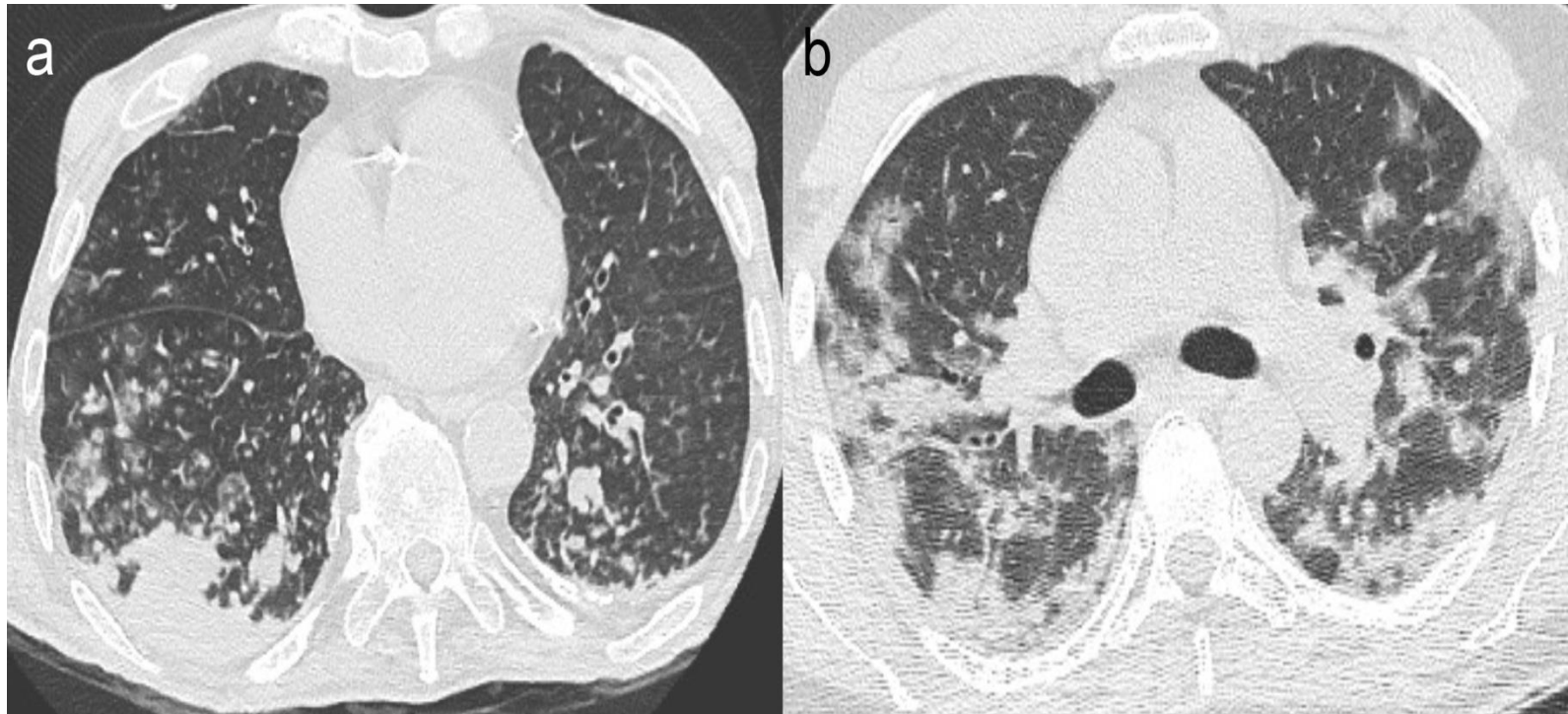
Axial HRCT images (a, b) in two different patients with uncommon findings of COVID-19 pneumonia due to emphysema. In a, an uncommon unilateral GG and consolidation with subpleural sparing due to paraseptal emphysema is nicely depicted. In b, mixed GG and consolidation areas, containing apparent cystic-like changes due to centrilobular emphysema, are evident predominantly in the right lung. Axial (c) and coronal (d) HRCT images of a 77-year-old male with COVID-19 pneumonia showing bilateral subpleural and peribronchovascular consolidations with mild GG. A 3- cm, subpleural, pseudonodular, part-solid lesion with cystic-like airspaces, irregular margins, and pleural retraction is detected in the posterior segment of the right upper lobe (arrowheads); a lung adenocarcinoma was suspected on the basis of morphological features and confirmed at biopsy.



Complications in two patients with severe COVID-19 pneumonia. In the first patient, axial HRCT image (a) demonstrates marked spontaneous pneumomediastinum and chest wall subcutaneous emphysema, associated with left pneumothorax. One week before, due to worsening dyspnoea, the patient had undergone CT scan with contrast medium injection to rule out pulmonary embolism (PE). Axial CT image (b) demonstrates a filling defect in the distal tract of the interlobar artery (arrowhead) due to acute PE. Note the shrinkage of the bilateral subpleural consolidations in the later CT scan (a). In the second patient, axial HRCT images (c, d) show focal consolidations with cavitation in the right upper lobe and some small consolidations in the left lung, superimposed on diffuse GG and septal thickening. A bacterial superinfection on COVID-19 pneumonia was suspected and the bronchoalveolar lavage confirmed a *Pseudomonas aeruginosa* infection.

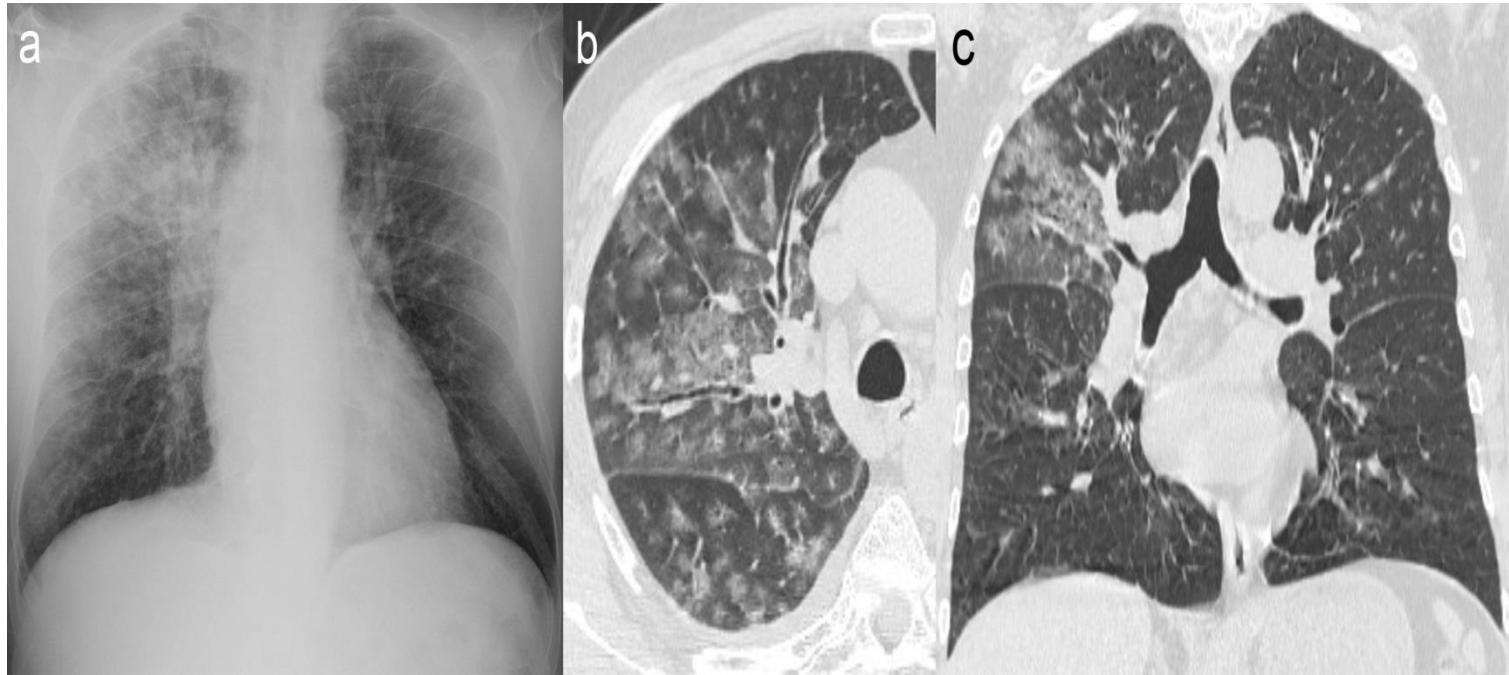


50-year-old male complaining of fever, chills and cough for 5 days. Chest X-ray (a) demonstrated a peripheral homogeneous opacity in the left upper lobe, suggestive of pneumonia with a sublobar nonsegmental appearance. Multiple RT-PCR tests resulted negative for SARS-CoV-2. Axial (b) and coronal (c) HRCT images confirm a peripheral sublobar nonsegmental consolidation with air bronchogram and mild adjacent GG in the left upper lobe. Microbiological tests were positive for *Streptococcus pneumoniae*.

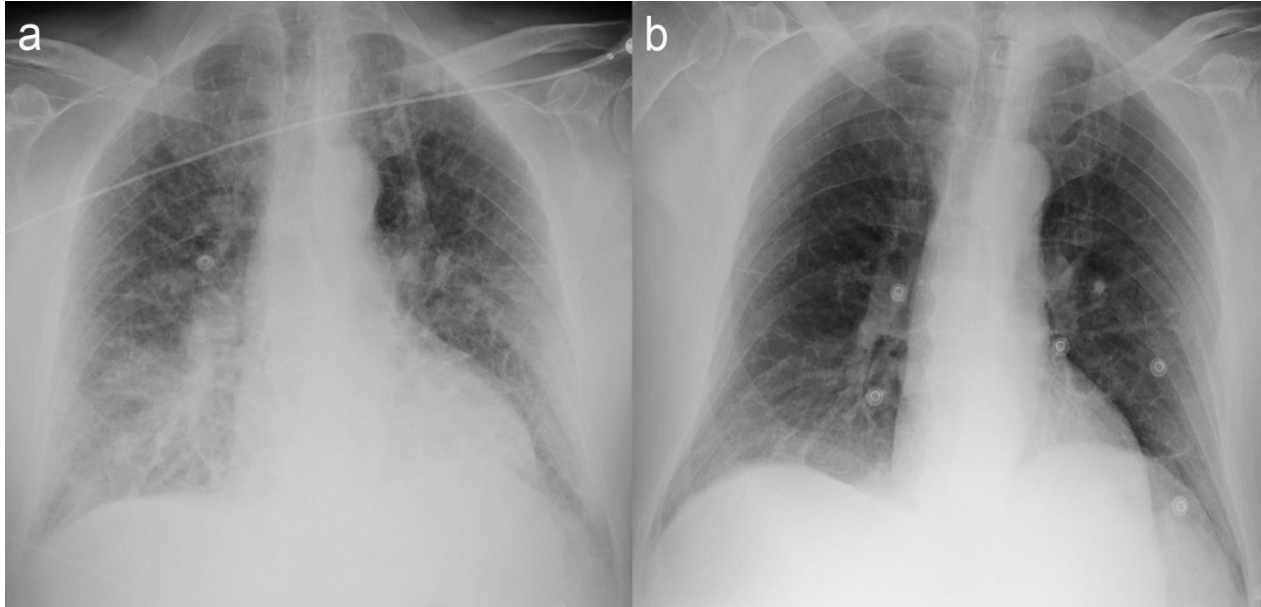


Axial HRCT images (a, b) in two different patients with a diagnosis of *Mycoplasma pneumoniae* pneumonia (a) and COVID-19 pneumonia (b), respectively.

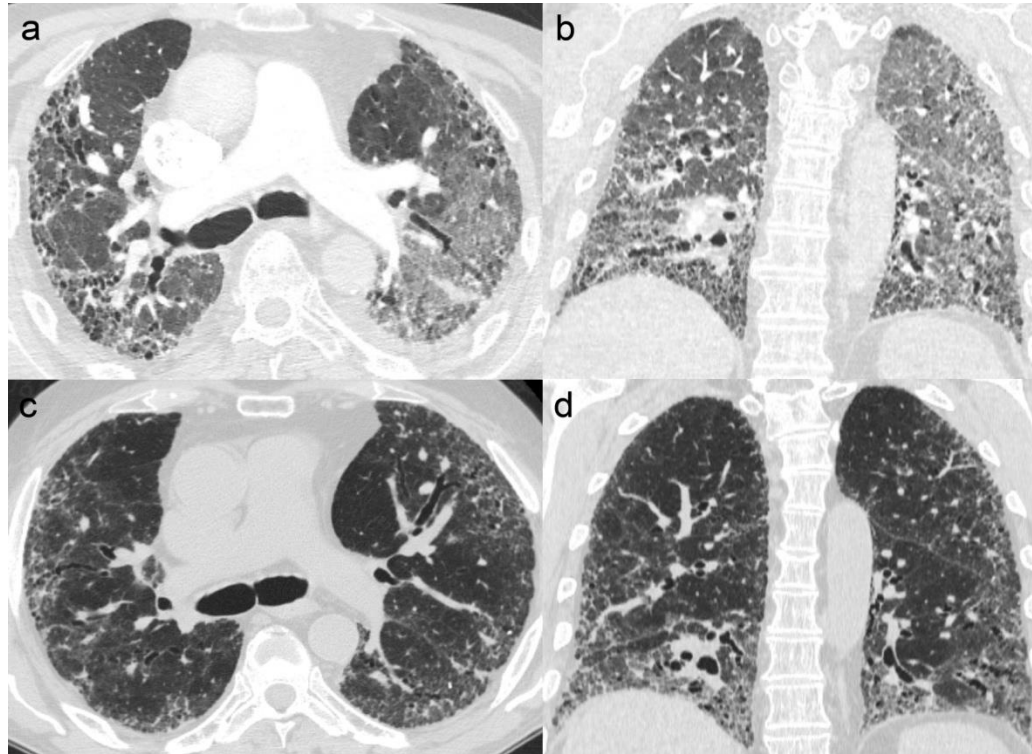
In a, patchy lobular and partially confluent consolidations and GG opacities, associated with centrilobular nodules and thickening of the peribronchovascular interstitium, are evident in the lower lobes. These findings allowed a confident differential diagnosis with COVID-19 pneumonia, shown in b, characterized by mixed GG and consolidations areas with a predominant peripheral/subpleural distribution in both lungs.



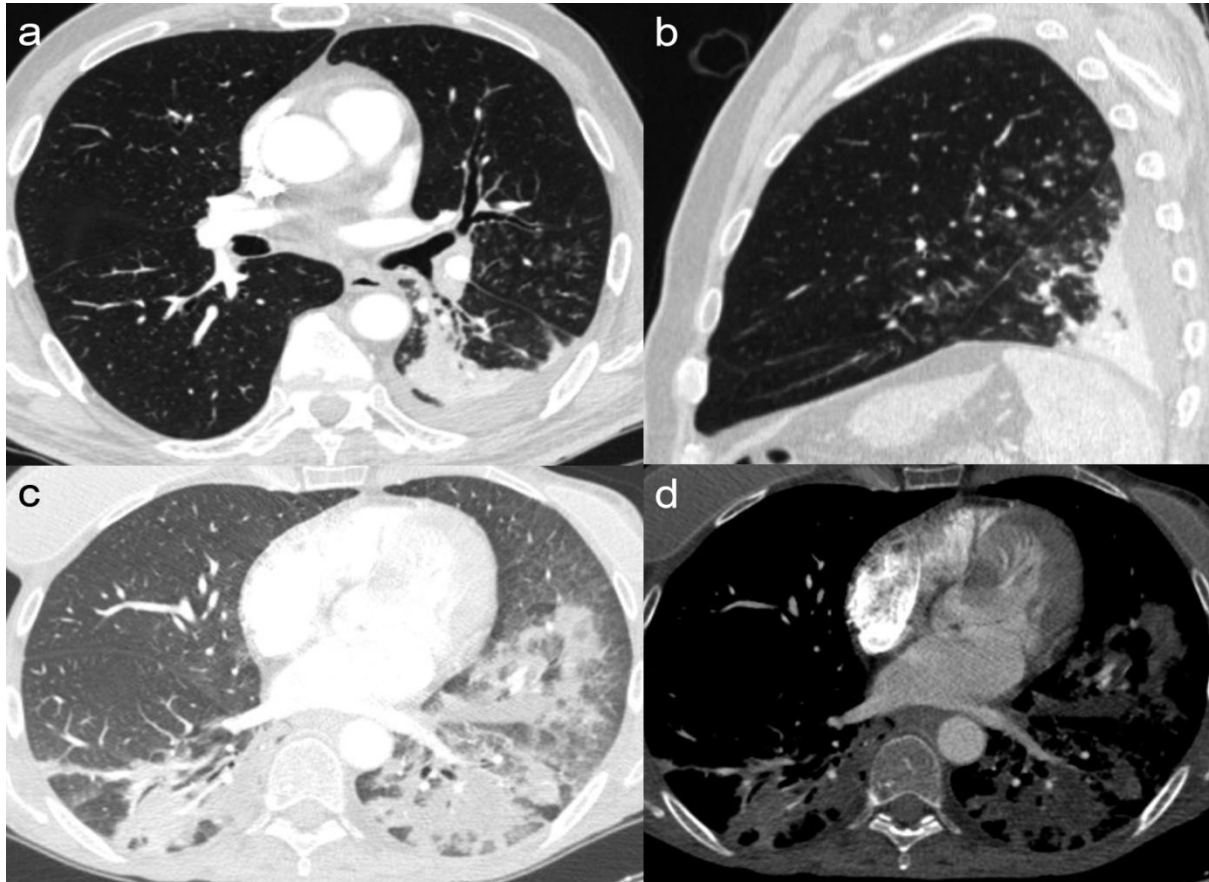
72-year-old male complaining of fever and dry cough. Chest X-ray (a) shows multiple confluent nodules and opacities in the mid-upper right lung, findings unlikely related to COVID-19 pneumonia. Axial (b) and coronal (c) HRCT images confirm the presence of multiple confluent centrilobular GG nodules and lobular areas in the right upper lobe and in the apical segment of the right lower lobe, suggestive of a bronchopneumonia pattern of infection, not related to COVID-19 pneumonia. Test was negative for SARS-CoV-2, while a diagnosis of Metapneumovirus pneumonitis was made



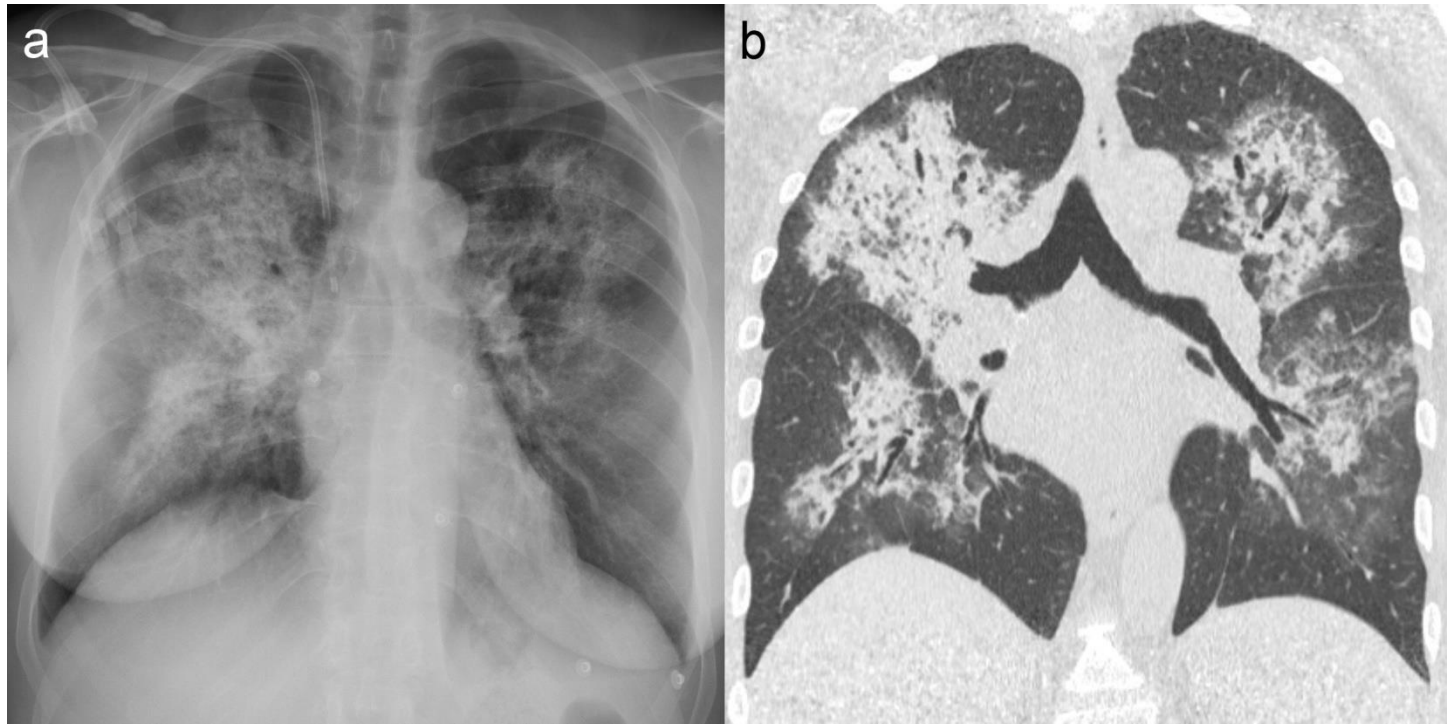
83-year-old male with history of acute coronary syndrome, complaining of severe dyspnoea and cough. The AP chest X-ray (CXR) at admission shows interstitial- alveolar opacities, with peribronchovascular and mid- basal distribution, associated with peribronchial cuffing, vessel blurring, prominence of the proximal pulmonary vessels and mild bilateral pleural effusion (a). A cardiogenic pulmonary oedema was suspected. Swab tests for COVID-19 were negative while high level of NT-proBNP (N-terminal-pro-B-type natriuretic peptide) was detected. Echocardiography showed reduced ejection fraction (35 %). The CXR performed after 5 days of treatment with diuretics demonstrates complete resolution of the pulmonary findings (b).



70-year-old male affected by connective tissue disease-Interstitial lung disease (CTD-ILD), admitted to the emergency department with worsening dyspnoea over the last two weeks; the patient presented with diffuse bilateral *velcro-like* crackles. The HRCT scan was performed with contrast administration to rule out PE. Axial (a) and coronal (b) HRCT images show bilateral diffuse GG opacities, more evident within the left lung, in areas not extensively involved by fibrotic changes. Comparison with the HRCT exam performed one year earlier (c, d) demonstrates the new onset of diffuse GG opacities. COVID-19 swab resulted negative and a diagnosis of acute exacerbation of pulmonary fibrosis was made.



HRCT images in two different patients with a diagnosis of aspiration pneumonia (a, b) and lipoid pneumonia (c, d), respectively. In the axial (a) and sagittal (b) images, a decumbent consolidation in the left lower lobe, associated with centrilobular micronodules and tree-in-bud opacities in the same lobe and in dorsal regions of the left upper lobe, is presented in a recumbent patient with recent tracheostomy. Note the left parapneumonic pleural effusion, which is an uncommon finding in COVID-19 pneumonia. In c, predominant peribronchovascular consolidations associated with mild *crazy paving* in the lower lobes and lingula, are shown in a patient with chronic use of vaseline. Note, in the mediastinal window image (d), the low attenuation values within consolidations, indicative of fat content (-40 HU). Distribution and attenuation of consolidations allowed an easy rule out of COVID-19 pneumonia.



62-year-old female affected by granulomatosis with polyangiitis (GPA) and chronic renal failure (note the ultrafiltration catheter on the right) admitted to the emergency department because of progressive shortness of breath over the last few days. Haemoptysis was not reported. AP chest X-ray (CXR) (a) demonstrates bilateral ill-defined opacities (more diffuse on the right), with peribronchovascular distribution and sparing of subpleural regions, apices and bases. Coronal HRCT image (b) shows bilateral confluent consolidations with the same distribution, associated with GG opacities, ill-defined centrilobular nodules and few septal thickening. On the basis of clinical data and radiological pattern, a diagnosis of diffuse alveolar haemorrhage was made. RT-PCR essay resulted negative for SARS-CoV-2.