

# European Radiology

## Imaging in the aftermath of COVID-19: What to expect

--Manuscript Draft--

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<b>Author Comments:</b>	Dear Prof. Menu,  Thank you for the positive comment on our editorial article entitled: "Imaging in the aftermath of COVID-19: What to expect". As suggested, we added a paragraph touching on the unclear correlation between imaging findings and clinical presentation. We strongly agree that this is a pivotal issue that needs to be addressed in future research studies. To date, data on the mid- and long term effects following a COVID-19 infection is scarce; however, we encounter substantial clinical late effects that are not well understood at the moment. Changes in the manuscript are highlighted in italic fonts. Also, we used the track changes function in Microsoft Word. We thank you for the opportunity to have our editorial considered for publication in the Journal European Radiology. We look forward to receiving your editorial decision.  Sincerely Yours, Lukas Ebner

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### Response to reviewers

Minor comments were as follow:

"It reads well, is concise, and addresses the issue of follow-up Covid-19. A critical note should be added regarding the correlation between imaging findings and clinical findings.

As far as we know, this relationship is still unclear. Patients with minimal findings on CT may show severe decline in lung function and patients with extensive diseases may have relatively normal lung function."

**Reply:** The authors would like to thank the editors of European Radiology for the positive feedback on this editorial note. In order to address the important point raised, the following paragraph was added to the manuscript, supported by an update reference [10]:

*Another critical aspect is the possible discrepancy between imaging findings and the clinical presentation of patients. To date, this relationship is still unclear. While some patients with minimal findings on chest CT may show a severe decline in lung function, there are patients with extensive diseases that exhibit relatively normal lung function. A correlation between imaging findings and moderate to severe disease course was identified on initial presentation [10], but focused and well-designed studies are needed to explore lung function loss and dynamic CT findings in mid- to long-term follow-up of COVID-19.*

10. Fang X, Li X, Bian Y, Ji X, Lu J (2020) Relationship between clinical types and radiological subgroups defined by latent class analysis in 2019 novel coronavirus pneumonia caused by SARS-CoV-2. *Eur Radiol* 30, 6139–6150

## Imaging in the aftermath of COVID-19: What to expect

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## Imaging in the aftermath of COVID-19: What to expect

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4 Dear editors  
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6 During the past six months, the COVID-19 pandemic has profoundly altered society and  
7 affected health care systems on a global scale. After initial reports of a new form of pneumonia  
8 in early 2020, the situation rapidly evolved into a worldwide phenomenon. The early experience  
9 with COVID-19 and its severe respiratory symptoms reinforce the role of radiology in the  
10 diagnosis and monitoring of patients. Since then, a plethora of reports and scientific studies  
11 focused on the critical role of imaging in the triage and diagnosis of patients [1]. We initially  
12 learned that the COVID-19 pneumonia does present with characteristic imaging findings in the  
13 acute stage [2,3]. Although not specific, these findings led to the broad use of either CT imaging  
14 or chest radiographs for the assessment of COVID-19. This was of particular interest since  
15 numerous studies observed increased false negative rates for RT-PCR and abnormal CT  
16 findings were detectable in otherwise asymptomatic individuals.  
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21 Since February 2020 with the first cases of the novel COVID-19 reported, the social, economic  
22 and particularly medical landscape has widely adapted to the new situation. In many countries,  
23 the so-called first wave of infections has diminished, but a gradual re-increase of infections  
24 can be expected for fall and winter. Simultaneously, the first patients that recovered from  
25 COVID-19 in early 2020 are now presenting with sequelae from the initial Sars-CoV-2 infection.  
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28 We are presently facing patients that recovered from acute COVID-19 pneumonia, some with  
29 ARDS, and that were discharged having recovered from the acute illness. Nevertheless, some  
30 of these patients report ongoing dyspnea and desaturate on exercise.  
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33 In the aftermath of a COVID-19 pneumonia, we observe in some patients with respiratory  
34 symptoms a suggestive pattern on CT images not previously reported in the context of COVID-  
35 19. In a subgroup of cured patients, we encounter a multifocal and/or apical predominant  
36 pattern of hypoattenuated areas in the lung parenchyma three months after discharge. These  
37 areas frequently involve several adjacent, secondary lobules that are sharply demarcated from  
38 the surrounding lung parenchyma. In some cases, ground glass bands circumscribing these  
39 hypoattenuated areas may be observed. This suspected geographic hyperinflation of  
40 pulmonary lobules is characterized by markedly decreased lung density. Additionally, in some  
41 cases, the perilobular septae are bulging towards the periphery, reinforcing the detectability  
42 and the authenticity of this pattern on inspiratory CT scans. This air trapping could also be  
43 confirmed on expiratory scans (Figure1), but we believe that the distinct morphology and  
44 significant decrease intensity may not require systematic use of expiratory CT scan protocols.  
45 In our experience, the identification of hyperinflated lobules inspiratory CT scans is facilitated  
46 by employing narrow window settings and minimal intensity projections on a series  
47 reconstructed with thin slices and soft-kernel (Figures 1, 2).  
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53 These CT findings are suggestive of small airways disease (SAD). In patients who initially  
54 suffered from ARDS, additional hallmark findings are reticulations, architectural distortions with  
55 bronchiectasis and curvilinear lines, as well as honeycombing in some cases. These CT  
56 features are attributable to sequelae of alveolar damage/ARDS and therefore less  
57 characteristic of COVID-19 *per se*. When added together, post-COVID-19 CT scans may  
58 resemble the so-called "head-cheese" sign described in chronic hypersensitivity pneumonitis,  
59 a disorder that primarily affects the peribronchial area.  
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1 In the follow-up of symptomatic post-COVID-19 patients, the reported signs are pivotal for the  
2 understanding of pathological mechanisms involved with SARS-CoV-2 infection. Based on the  
3 CT patterns we encountered in cured COVID-19 patients, we noticed that some patients  
4 display a SAD predominance, while others present a predominance of classical fibrotic  
5 changes or a mixed type pattern. Of note, SAD was also reported in previous MERS, SARS  
6 and severe influenza infection and ARDS [4,5,6]. A limiting factor of our findings is that not all  
7 patients initially received a baseline CT and we can therefore not completely rule out  
8 preexisting conditions such as SAD.  
9

10 These preliminary findings highlight the importance of imaging not only in the acute setting,  
11 but also in the follow-up of COVID-19. As we adapt to the pandemic, the death toll is declining  
12 and hopefully mild to moderate infections will continue to surpass severe cases. Nevertheless,  
13 health care providers will face patients afflicted with long-term impairment. We suggest to  
14 scrutinize post-COVID-19 CT scans for findings of mosaic pattern, likely representing air  
15 trapping, and indicative of a potential distal airway obstruction. Future research should further  
16 address the complex association of SAD and reported vascular involvement [7,8]. It has to be  
17 determined if and to what degree microvascular thrombosis may contribute to bronchiolar  
18 constriction or SAD [9].  
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23 Another critical aspect is the possible discrepancy between imaging findings and the clinical  
24 presentation of patients. To date, this relationship is still unclear. While some patients with  
25 minimal findings on chest CT may show a severe decline in lung function, there are patients  
26 with extensive diseases that exhibit relatively normal lung function. A correlation between  
27 imaging findings and moderate to severe disease course was identified on initial presentation  
28 [10], but focused and well-designed studies are needed to explore lung function loss and  
29 dynamic CT findings in mid- to long-term follow-up of COVID-19.  
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33 In the light of increasing numbers of patients suffering late effects of COVID-19, we emphasize  
34 the importance of longitudinal evaluation to assess potential reversibility of the observed CT  
35 patterns.  
36

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38 The authors state that this work has not received any funding.  
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### 41 ***Compliance with Ethical Standards***

#### 42 ***Guarantor:***

43 The scientific guarantor of this publication is C. Beigelman-Aubry.  
44  
45

#### 46 ***Conflict of Interest:***

47 The authors of this manuscript declare no relationships with any companies, whose products  
48 or services may be related to the subject matter of the article.  
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#### 51 ***Statistics and Biometry:***

52 No complex statistical methods were necessary for this paper.  
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1 **Informed Consent:**

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3 Written informed consent was not required for this study because of editorial purpose.

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6 **Ethical Approval:**

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9 Institutional Review Board approval was not required.

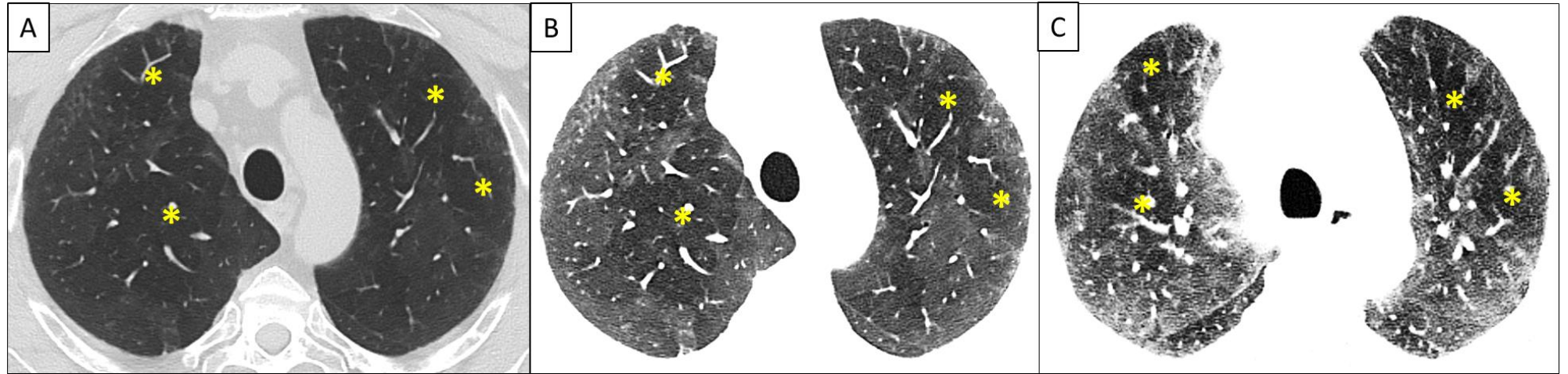
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12 **Methodology**

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14 Methodology:  
15 Editorial comment

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19 **References**

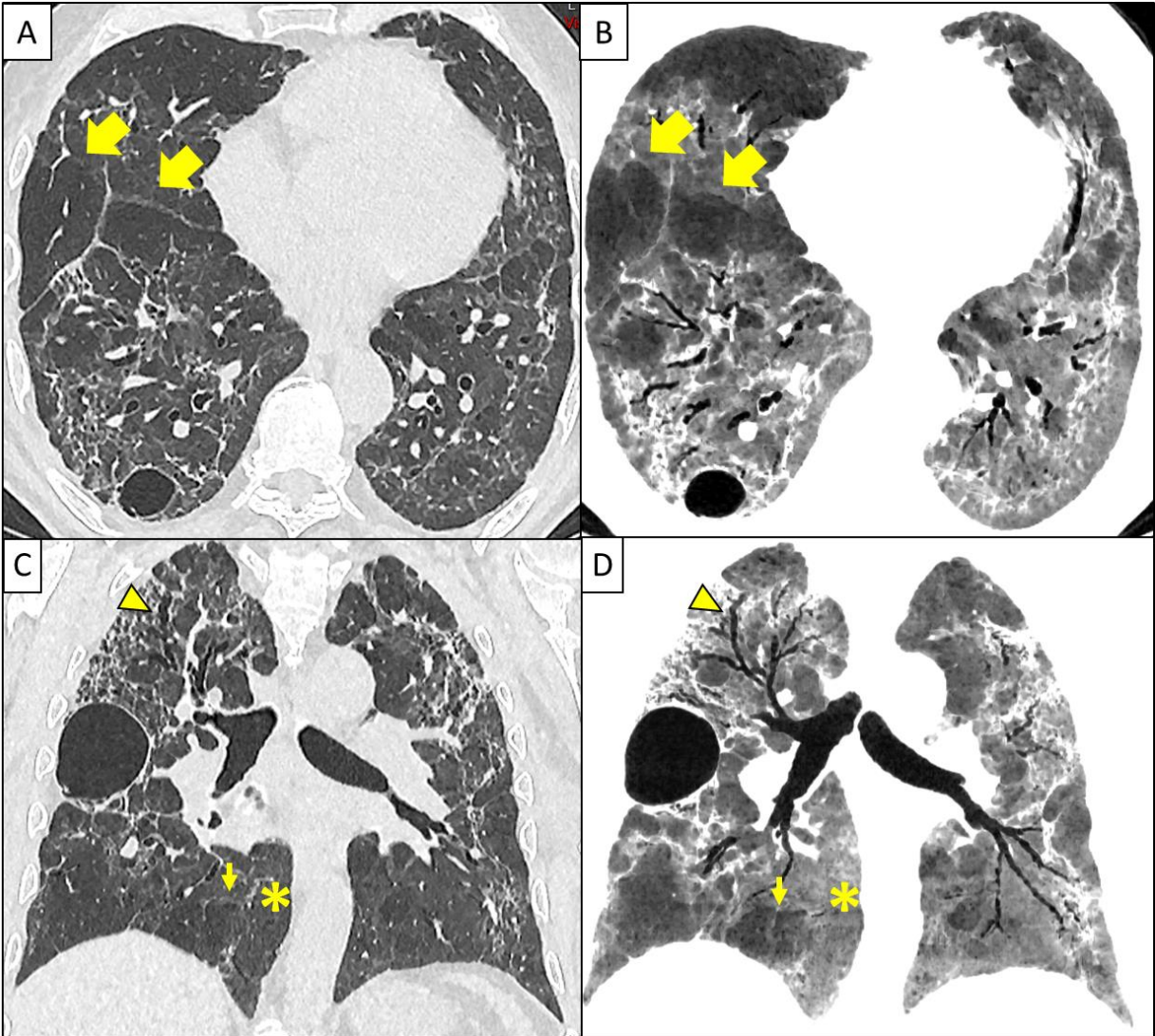
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21 **Figure 1.** Three-month follow-up CT scan of a patient after COVID-19 pneumonia presenting with exertional dyspnea. Sharply demarcated areas of  
22 hypoattenuating lung parenchyma are depicted in both upper lobes (A). Reading the same acquisition on inspiration with narrow window settings on  
23 a series reconstructed in thin slices with soft kernel facilitates the detection of these abnormal areas and enforce a mosaic-like attenuation pattern  
24 (B). An additionally performed expiratory scan confirms the SAD owing to air trapping that matches with several hypoattenuating areas detected in  
25 B. Note the predominant hypoattenuation pattern in this case.  
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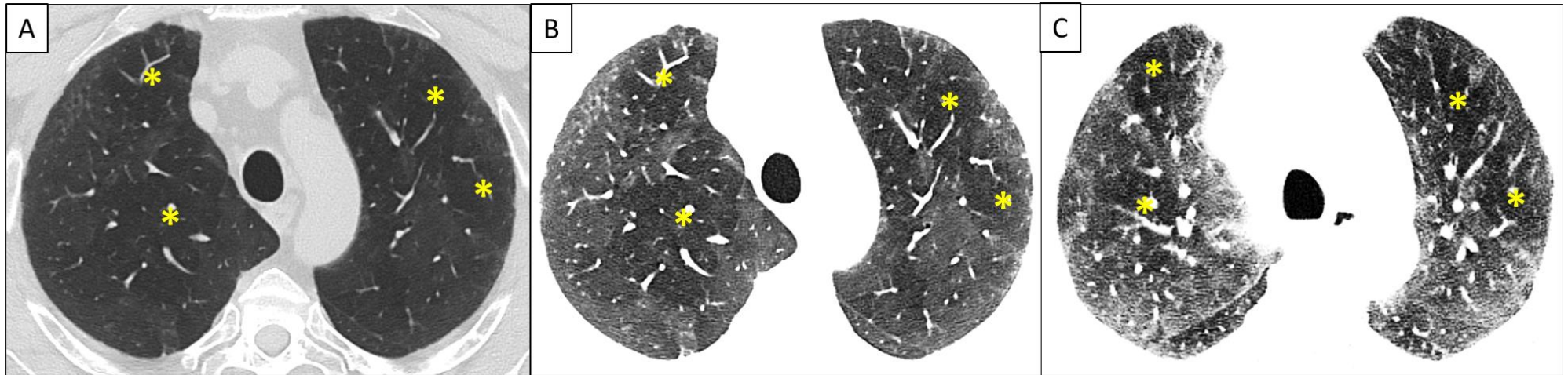


**Figure 2.** Three-months after COVID-19 and ARDS, CT shows severe architectural distortion and traction bronchiectasis (arrowhead in C and D). These findings are frequent in patients that recovered from ARDS. However, multi-lobular hypoattenuation pattern is also present (arrows) on axial 1mm-thick slices reconstructed with lung kernel (A) and 10 mm-thick minimum intensity projections (mIP) slices with soft kernel (B), and on coronal reformats 1mm-thick reconstructed with lung kernel (C) and 10 mm-thick minimum intensity projections with soft kernel (D). The mIP post-processing (B,D) highlights a geographic, lobular hypoattenuation pattern that most likely represents multifocal small airways disease. Presumably hyperinflated lobules further exhibit convex perilobular septae towards normal lung parenchyma (small arrows), that should correspond to an air trapping on expiration. Note that the normal lung parenchyma (stars) is more easily assessed on mIP reformats with narrow window settings (B,D), than on classical lung analysis (A,C). Note pneumatoceles in subpleural location described in COVID-19 pneumonia as well.

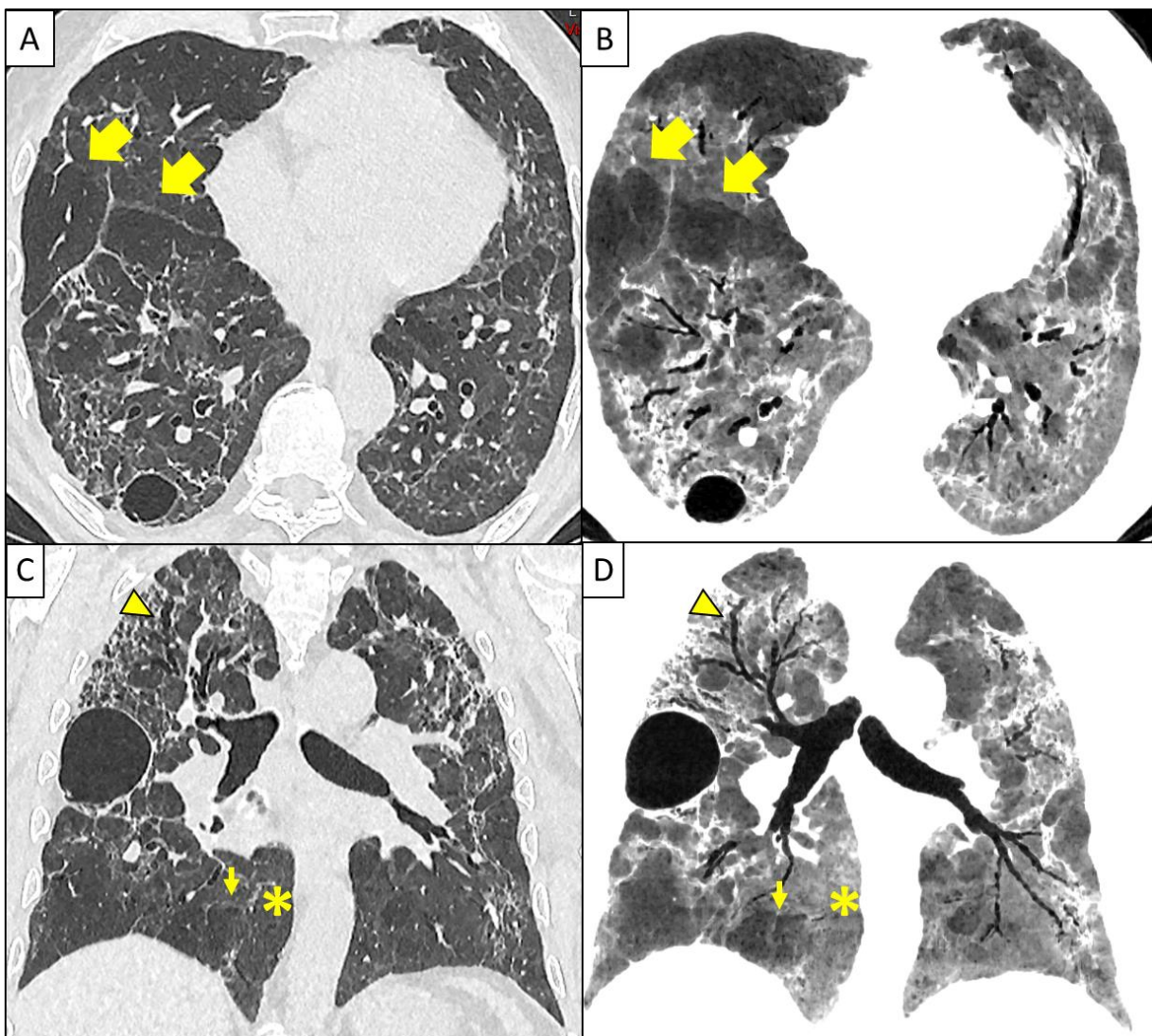




**Figure 1.** Three-month follow-up CT scan of a patient after COVID-19 pneumonia presenting with exertional dyspnea. Sharply demarcated areas of hypoattenuating lung parenchyma are depicted in both upper lobes (A). Reading the same acquisition on inspiration with narrow window settings on a series reconstructed in thin slices with soft kernel facilitates the detection of these abnormal areas and enforces a mosaic-like attenuation pattern (B). An additionally performed expiratory scan confirms the SAD owing to air trapping that matches with several hypoattenuating areas detected in B. Note the predominant hypoattenuation pattern in this case.



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***Compliance with Ethical Standards******Guarantor:***

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***Conflict of Interest:***

The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

***Statistics and Biometry:***

No complex statistical methods were necessary for this paper.

***Informed Consent:***

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***Ethical Approval:***

Institutional Review Board approval was not required.

***Methodology***

Methodology:  
Editorial comment

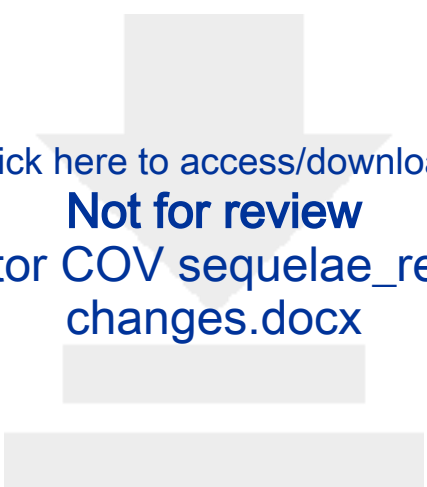


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