Chest CT–based Assessment of 1-year Outcomes after Moderate COVID-19 Pneumonia

Marialuisa Bocchino, MD, PhD • Roberta Lieto, MD • Federica Romano, MD • Giacomo Sica, MD • Giorgio Bocchini, MD • Emanuele Muto, MD • Ludovica Capitelli, MD • Davide Sequino, MD • Tullio Valente, MD • Giuseppe Fiorentino, MD • Gaetano Rea, MD

From the Respiratory Medicine Section, Department of Clinical Medicine and Surgery, Federico II University of Naples, Via S Pansini 5, 80131 Naples, Italy (M.B., L.C., D.S.); and Department of Radiology (R.L., E.R., G.S., G.B., E.M., T.V., G.R.) and Pathophysiology and Respiratory Rehabilitation Department of Critical Area (G.F.), Monaldi Hospital, AO dei Colli, Naples, Italy. Received January 6, 2022; revision requested March 7; revision received April 13; accepted April 25.

Address correspondence to M.B. (email: marialuisa.bocchino@unina.it).

Conflicts of interest are listed at the end of this article.

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Background: COVID-19 pneumonia may lead to pulmonary fibrosis in the long term. Chest CT is useful to evaluate changes in the lung parenchyma over time.

Purpose: To illustrate the temporal change of lung abnormalities on chest CT scans associated with COVID-19 pneumonia over 1 year.

Materials and Methods: In this prospective study, patients previously hospitalized due to COVID-19 pneumonia who visited the radiology department of a tertiary care center for imaging follow-up were consecutively enrolled between March 2020 and July 2021. Exclusion criteria were acute respiratory distress syndrome, requirement of intubation and/or mechanical ventilation, pulmonary embolism, and any interstitial lung disease. High-resolution volumetric noncontrast chest CT scans were acquired at 3, 6, and 12 months from the first diagnosis and were compared with baseline CT scans. The imaging features analyzed were ground-glass opacity (GGO), consolidation, pleuroparenchymal band, linear atelectasis, bronchiecasis and/or bronchiolectasis, reticulation, traction bronchiectasis and/or bronchiolectasis, and honeycombng. The prevalence distribution of lung abnormalities was recorded at all time points.

Results: Eighty-four participants (56 men; mean age, 61 years ± 11 [SD]) were studied. GGOs and consolidations represented the main baseline lung abnormalities, accounting for a median severity score of 9 (IQR, 7–12.7; maximum possible score, 20), which indicates moderate lung involvement. The baseline prevalence of GGOs decreased from 100% to 2% of participants at 1 year, and that of consolidations decreased from 71% to 0% at 6 months. Fibrotic-like abnormalities (pleuroparenchymal bands, linear atelectasis, bronchiecasis and/or bronchiolectasis) were detected at 3 months (50% of participants), 6 months (42% of participants), and 1 year (5% of participants). Among these, pleuroparenchymal bands were the most represented finding. Fibrotic changes (reticulation and traction bronchiectasis and/or bronchiolectasis) were detected at 3–6 months (2%) and remained stable at 1 year, with no evidence of honeycombing. At 1 year, lung abnormalities due to COVID-19 pneumonia were completely resolved in 78 of 84 (93%) participants.

Conclusion: Residual lung abnormalities in individuals hospitalized with moderate COVID-19 pneumonia were infrequent, with no evidence of fibrosis at 1-year chest CT.

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COVID-19 is a systemic disorder that has strained the medical and scientific community since the first wave of the pandemic due to the spread of SARS-CoV-2. The lung is the most frequently affected site and, as a vital organ, represents an important organ to evaluate for possible sequelae in the long term (1). Recently, the U.K. National Institute for Health and Care Excellence differentiated three clinical phases from the time of initial diagnosis: acute (within 4 weeks), ongoing (from 4 to 12 weeks), and long COVID-19 (more than 12 weeks), with the last phase potentially involving various organs (2–4).

The long-term consequences of COVID-19 are an issue of concern because residual breathlessness and reduced exercise tolerance negatively impact quality of life. In this context, it has been hypothesized that COVID-19 pneumonia may evolve into pulmonary fibrosis with permanent organ damage (4,5). Postviral syndrome is well documented, and similar concerns had emerged during the severe acute respiratory syndrome and Middle East respiratory syndrome outbreaks (6). However, pulmonary fibrosis was rare (<5%). Certainly, if the clinical-radiologic evidence confirms the occurrence of post-COVID-19 pulmonary fibrosis, even as a less common complication, a very worrisome public health scenario would appear given the huge number of affected individuals.

Two additional aggravating factors are acute respiratory distress syndrome (ARDS) and barotrauma in mechanically ventilated patients, with the latter having an incidence of up to 40% (7–10). In addition, patients affected by any interstitial lung disease who develop SARS-CoV-2–related pneumonia deserve special attention (11,12). Indeed, similar to other infections, SARS-CoV-2 infection may act as a triggering factor for the acute exacerbation and/or progression of interstitial lung disease (13). On the other hand, the incidental finding of subclinical interstitial lung disease because of the occurrence of COVID-19 is an emerging
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Abbreviations
ARDS = acute respiratory distress syndrome, GGO = ground-glass opacity

Summary
In this longitudinal study of patients who had been hospitalized with moderate-severity COVID-19 pneumonia, 93% of participants had complete resolution of baseline lung abnormalities at 12-month chest CT.

Key Results
- In a prospective study of 84 participants with moderate COVID-19 pneumonia, baseline chest CT ground-glass opacities (GGOs) and consolidations gradually decreased over time, with GGOs being present in 2% of participants at 1 year.
- Fibrotic-like abnormalities (pleuroparenchymal bands, linear atelectasis, and bronchiectasis and/or bronchiolectasis) became appreciable at 3 months (50%) and were infrequent at 12 months (5%).
- Fibrotic changes (eg, reticulation and traction bronchiectasis and/or bronchiolectasis) were detected at 3–6 months (2%) and persisted at 1 year; no honeycombing was observed.

Summary
ARDS = acute respiratory distress syndrome, GGO = ground-glass opacity

Materials and Methods

Study Design and Participants
The prospective study was performed according to the amended Declaration of Helsinki, and all participants provided written informed consent. The study was approved by the local institutional ethics committee (protocol number 0021131/2020). Inclusion criteria were previous hospitalization and diagnosis of COVID-19 pneumonia confirmed by means of a SARS-CoV-2–positive polymerase chain reaction test via nasopharyngeal swabs. Patients who underwent subsequent follow-up at our radiology department in a tertiary center were consecutively involved in the study have 10–20 years of experience in the field of thoracic radiology.

Imaging Analysis
The baseline extent of alterations of COVID-19 pneumonia was quantified as follows: for each of the five lobes, lung involvement was reported as none (0%, score 0), minimal (1%–25%, score 1), mild (26%–50%, score 2), moderate (51%–75%, score 3), or severe (76%–100%, score 4). The total severity score was reached by summing the five lobe scores, with a range of 0–20 as per Chung et al (15). CT scans were independently reviewed by three radiologists (G.R., G.S., and T.V.) blinded to CT findings. In the case of discordant scores among the observers, the average value arising from the sum of individual evaluations was chosen for final scoring. Multiplanar reconstruction was used to resolve any interpretation doubt. Postacute lung alterations during the follow-up period were described according to conventional radiologic characteristics and recorded for each patient at each study time point. Specifically, CT features included ground-glass opacity (GGO), consolidation, linear atelectasis, pleuroparenchymal band, bronchiectasis and/or bronchiolectasis, reticulation, traction bronchiectasis and/or bronchiolectasis, and honeycombing, as defined in the Fleischner Society glossary (16). The location and extent (diffuse vs focal) of CT alterations were assessed as well. All follow-up CT scans were independently analyzed at the same time as the previous scans available and collectively discussed for consensus before data analysis (G.R., G.S., T.V., R.L., F.R., G.B., and E.M.). All radiologists involved in the study have 10–20 years of experience in the field of thoracic radiology.

Statistical Analysis
Numerical variables are described using means ± SDs if normally distributed or medians and IQRs (25th and 75th percentiles). Categorical variables are summarized using absolute frequencies and percentages. Descriptive statistics were analyzed using a commercially available package (SPSS release 21.0; 2016; SPSS).

Results

Participant Characteristics
Overall, the study group was composed of 84 participants with a mean age of 61 years ± 11 (SD). Of the 84 participants, 56 were men (67%). Demographic and baseline clinical characteristics are reported in Table 1. As shown, 49 participants were never-smokers (58%) and systemic arterial hypertension was the most prevalent comorbidity (55 of 84 participants, 65%). The median body mass index was 27.3 kg/m², with approximately

and intriguing clinical scenario that further complicates the interaction of SARS-CoV-2 with the lung.

Chest CT is essential for disease monitoring, with timing being a crucial factor to fully assess the ability of lung recovery. To determine the natural history of pulmonary involvement in COVID-19, our study aimed to illustrate the temporal change of lung abnormalities at chest CT during 1-year follow-up of individuals previously hospitalized due to COVID-19 pneumonia.

High-Resolution CT of the Chest
High-resolution chest CT scans were acquired at 3, 6, and 12 months from the time of the first diagnosis and retrospectively compared with CT images acquired on hospital admission. Standard full-dose volumetric noncontrast scans were obtained with a 64-section multidetector CT scanner (MDCT 64; GE Medical Systems), with participants in the supine position during a breath hold following full inspiration. The scanning parameters were 120–140 kV and 100–200 mAs, with the smallest field of view possible according to the body habitus. A low-dose protocol (80–100 kV and 50 mAs) was preferred in normal-weight participants younger than 55 years (14). Volume CT dose index and dose-length product ranged from 3.2 to 6.2 mGy and 133 to 288 mGy/cm, respectively. The matrix size was 512 × 512 pixels; images were reconstructed with a 1- or 1.25-mm section thickness using a bone filter. A soft-tissue reconstruction filter was additionally used to identify thoracic findings in the mediastinal window.

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one-third of the study sample (24 of 84 participants, 29%) being represented by obese participants. The median CT severity score was 9 (out of 20), which is suggestive of moderate lung involvement. During previous hospitalization, all participants required oxygen supplementation (nasal cannula or Venturi mask). High-flow nasal cannula and continuous positive airway pressure were adopted in 21 and 18 participants (25% and 21%, respectively), whereas noninvasive ventilation was required in six (7%). All participants received systemic steroids and prophylactic low-molecular-weight heparin. Antiviral agents (mainly remdesivir) were used in 24 of the 84 participants (27%).

### Participants with Moderate COVID-19 Pneumonia Had a High Rate of Recovery at 1-year Follow-up

As shown in Table 2, baseline chest CT features of COVID-19 pneumonia mainly comprised GGOs and consolidations, with a diffuse distribution in 96% and 42% of CT scans analyzed, respectively. Focal consolidations were reported in 35 participants, with a marked predilection for the lower lung lobes (89%). At 3-month follow-up, the prevalence of diffuse GGOs was still high (94%); conversely, the frequency of consolidations dropped from 71% at baseline to 13%, and those persisting were focally limited to the lower lobes. At the 6-month check-up, GGO was still detectable in 20% of participants (17 of 84), whereas consolidations disappeared in all participants. Residual GGO was appreciable in 2% of participants (two of 84) at the end of the study.

Chest CT findings in postacute COVID-19 pneumonia were classified into fibrotic-like or fibrotic abnormalities, as listed in Table 3. As shown, fibrotic-like changes included pleuroparenchymal bands, linear atelectasis, and bronchiectasis and/or bronchiolectasis. They became appreciable in 42 participants at 3-month follow-up, with an overall prevalence of 50%. Pleuroparenchymal bands, which had an organizing pneumonia-like pattern, were the most represented fibrotic-like change (36 of 42, 86%). They mainly had a focal distribution (67%) and were characteristically restricted to the lower lung lobes in all participants. Linear atelectasis, mainly located in the lower subpleural regions, and bronchiectasis and/or bronchiolectasis (in close proximity to consolidation areas) were reported in eight and two participants, accounting for a prevalence of 19% and 5%, respectively. Fibrotic-like abnormalities were still present at 6-month follow-up in 35 of the 84 participants (42%); however, the frequency of pleuroparenchymal bands decreased to 57% (20 of 35 participants), with most persisting in the lower lobes (60%). Frequencies of linear atelectasis and bronchiectasis and/or bronchiolectasis increased to 34% (12 of 35 participants) and 20% (seven of 35 participants), respectively, at 6 months.

Fibrotic abnormalities also became evident at 3-month follow-up, and the prevalence of subpleural reticulation in the lower lung lobes was 2% (two of 84 participants). This prevalence remained stable at 6 months, along with the appearance of traction bronchiectasis and/or bronchiolectasis in the same two participants with previous evidence of reticulation (2%). Honeycombing was not detected at any of these time points. Overall, at 1-year follow-up, residual fibrotic-like abnormalities were present in four of the 84 participants (5% prevalence). Fibrotic abnormalities (reticulation in combination with traction bronchiectasis and/or bronchiolectasis) remained stable in the same two participants (2%), along with residual GGO and no honeycombing. Finally, a normal CT appearance was recorded in 34 of the 84 participants (42%) at 6 months and in 78 (93%) at 1-year follow-up. Representative examples of the chest CT temporal sequence of lung alterations of postacute COVID-19 pneumonia are shown in Figures 1–4.

### Discussion

At present, there is no definite evidence that COVID-19 pneumonia uncomplicated by acute respiratory distress syndrome (ARDS) evolves into pulmonary fibrosis. The purpose of this study was to evaluate longitudinal changes during the course of healing of COVID-19 pneumonia over a 1-year period. We included patients who had previously been hospitalized for SARS-CoV-2 infection.

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**Table 1: Demographic Characteristics and Baseline Clinical Features of the Study Participants**

| Parameter                      | Value |
|--------------------------------|-------|
| No. of participants           | 84    |
| Age (y)*                      | 61 ± 11 |
| No. of men                    | 56 (67) |
| Never-smokers                 | 49 (58) |
| BMI (kg/m²)†                  | 27.3 (25–30.8) |
| Type II diabetes              | 23 (27) |
| Arterial systemic hypertension| 55 (65) |
| Cardiovascular diseases       | 17 (20) |
| Chronic lung diseases‡        | 7 (8) |
| Obesity                       | 24 (29) |
| C-reactive protein level (mg/dL)† | 6.2 (3.3–9.6) |
| d-dimer level (ng/mL)†        | 280 (178–468) |
| Blood neutrophil-to-lymphocyte ratio† | 10.3 (6.9–18.9) |
| Pao2/Fio2 ratio‡              | 192 ± 96 |
| Lung severity score†          | 9 (7–12.7) |
| Oxygen supply                 | 84 (100) |
| (nasal cannula or Venturi mask)|       |
| HFNC                           | 21 (25) |
| CPAP                           | 18 (21) |
| NIV                            | 6 (7) |
| Systemic steroids§             | 84 (100) |
| Antiviral agents§             | 24 (27) |
| LMWH prophylaxis               | 84 (100) |
| Length of hospitalization (d)§ | 16 (10–23) |

Note.—Except where indicated, data are numbers of participants, with percentages in parentheses. BMI = body mass index, CPAP = continuous positive airway pressure, Fio2 = fraction of inspired oxygen, HFNC = high-flow nasal cannula, LMWH = low-molecular-weight heparin, NIV = noninvasive ventilation.

* Data are means ± SDs.
‡ Data are medians, with IQRs in parentheses.
§ Included chronic obstructive pulmonary disease and bronchial asthma.
* Obtained at hospital admission.
† Methylprednisolone or dexamethasone.
‡ Lopinavir and/or ritonavir or remdesivir.
and who had a baseline CT scan. We excluded patients who developed ARDS during hospitalization or who required intubation or mechanical ventilation. The overall severity of COVID-19 pneumonia in this study sample was considered to be moderate (median lung CT severity score, 9 out of a maximum score of 20). Our results showed that postinflammatory changes after COVID-19 pneumonia slowly resolved over the subsequent 12 months, with 78 of the 84 participants (93%) having complete resolution of baseline CT changes at 12 months.

GGOs and consolidations were the main alterations at disease presentation, with a preferential distribution in the lower lobes for focal abnormalities. The prevalence of GGO decreased from 100% at baseline to 20% at 6 months and 2% at 1 year, along with a complete disappearance of consolidations. Fibrotic abnormalities (reticulation and traction bronchiectasis and/or bronchiolectasis) were detectable in two of the 84 participants (2%) beginning at the 3-month CT scan and remained unchanged in appearance at the 1-year CT scan without evidence of honeycombing. The centrifugal distribution resembled the CT pattern of fibrosing organizing pneumonia and/or nonspecific interstitial pneumonia (17,18). Further evolution of these abnormalities remains a question that cannot be answered at the moment. Because the prevalence of pre-existing interstitial lung abnormalities might be up to 5% in our study sample (19), lung abnormalities observed at 12 months may have been present before the baseline CT scan at the onset of SARS-CoV-2 infection.

Wu et al (20) recently reported that lung function and exercise tolerance improved in 83 patients with COVID-19 at 1 year from hospitalization. However, residual GGOs were still detectable in 24% of the study sample and were associated with baseline CT extent (20). In a retrospective cohort of 201 patients with COVID-19, Yasin et al (21) identified two subgroups of survivors: a fibrotic group, with evident fibrosis, and a nonfibrotic group, without evident fibrosis. The average CT follow-up time after discharge was 41.5 days, and fibrosis (48.1% of the study sample) was defined as parenchymal bands, irregular interfaces, coarse reticular patterns, and traction bronchiectasis. Patient age, CT severity score at baseline, consolidation and/or crazy-paving score, and intensive care unit admission were independent risk factors for fibrosis (21). Similar data were reported in other COVID-19 cohorts early after hospital discharge (21,22).

Additional studies with longer monitoring (maximum, 6 months) are available. In a prospective cohort of 173 participants with moderate to severe COVID-19 pneumonia, pulmonary fibrosis occurred in 90 participants (52%) 3 months after hospital discharge and correlated with CT extent at presentation. Forty-one of 62 participants who underwent chest CT at 6 months (66.1%) showed no considerable changes in fibrotic findings (ie, parenchymal bands and interlobular septal thickening), while 21 (33.9%) had diminished lung fibrosis (23). Persistent GGO was detected in 30.8% of the 117 patients evaluated by Aul et al (24) at 6 months, with concomitant traction bronchiectasis in 9.3%. Pulmonary fibrosis (parenchymal bands, irregular interfaces, reticulation, and traction bronchiectasis) was more likely to develop after 120 days from discharge in older patients with higher body mass index, severe disease, longer viral clearance time, and delayed hospitalization in the study by Li et al (25). Similarly, consolidations and reticulations have more recently been described at 6-month follow-up in older patients with longer hospital stay (20% of the study sample) (26). Han et al (27) reported that 40 of 114 (35%) patients had fibrotic-like changes (parenchymal bands, traction bronchiectasis, and/or honeycombing) at 6-month follow-up. Of note, ARDS (63% of participants) was an independent predictor of fibrosis, as confirmed in autopsy studies (28).

Two elements substantially differentiate these findings from our experience. Timing is a critical factor because lung recovery may occur slowly and improvement over time cannot be excluded. The postulated activation of profibrogenic pathways alone is not necessarily evidence of ongoing fibrosis but should be framed in the expected consequential tissue repair processes. Second, the inclusion of patients in the intensive care unit is by itself a bias, as a causal relationship between residual CT abnormalities and mechanical ventilation–related lung damage cannot

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**Table 2: Chest CT Features of COVID-19 Pneumonia during 1-year Follow-up**

| CT Finding                     | Baseline CT | 3-month CT | 6-month CT | 12-month CT |
|-------------------------------|-------------|------------|------------|-------------|
| Ground-glass opacity          | 84/84 (100) | 79/84 (94) | 17/84 (20) | 2/84 (2)    |
| Diffuse                       | 81/84 (96)  | 74/79 (94) | 8/17 (47)  | 1/2 (50)    |
| Focal                         | 3/84 (4)    | 5/79 (6)   | 9/17 (53)  | 1/2 (50)    |
| Consolidation                 | 60/84 (71)  | 11/84 (13) | 0          | 0           |
| Diffuse                       | 25/60 (42)  | 4/11 (36)  | 0          | 0           |
| Focal                         | 35 (58)     | 7/11 (64)  | 0          | 0           |

Note.—Data are numerators and denominators, with percentages in parentheses.

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**Table 3: Chest CT Findings of Post-Acute COVID-19 Pneumonia during 1-year Follow-up**

| CT Finding                          | Baseline CT | 3-month CT | 6-month CT | 12-month CT |
|-------------------------------------|-------------|------------|------------|-------------|
| Fibrotic-like abnormalities         | 0           | 42/84 (50) | 35/84 (42) | 4/84 (5)    |
| Pleuroparenchymal band              | 0           | 36/42 (86) | 20/35 (57) | 3/4 (75)    |
| Linear atelectasis                  | 0           | 8/42 (19)  | 12/35 (34) | 2/4 (50)    |
| Bronchiectasis and/or bronchiolectasis | 0       | 2/42 (5)   | 7/35 (20)  | 2/4 (50)    |
| Fibrotic abnormalities              | 0           | 2/84 (2)   | 2/84 (2)   | 2/84 (2)    |
| Reticulation                        | 0           | 2/2 (100)  | 2/2 (100)  | 2/2 (100)   |
| Traction bronchiectasis and/or bronchiolectasis | 0  | 0           | 2/2 (100)  | 2/2 (100)   |
| Honeycombing                        | 0           | 0          | 0          | 0           |
| Normal CT appearance                | 0           | 34/84 (40) | 78/84 (93) |             |

Note.—Data are numerators and denominators, with percentages in parentheses.
Figure 2: High-resolution noncontrast chest CT findings in a 70-year-old man with COVID-19 pneumonia and previous mitral valve replacement during 1-year follow-up. (A) Archive control noncontrast CT axial section obtained 1 year before COVID-19 shows the absence of any focal or diffuse lung disease (box). (B) Baseline image obtained at the onset of COVID-19 pneumonia shows bilateral consolidations (box) in the lower lung lobes (lung severity score, 12 out of 20). (C) Image obtained at 6-month follow-up shows almost complete reabsorption of consolidations. Mild GGOs are detectable in the lower lobes, and there is evidence of linear atelectasis (box). (D) Image obtained at 1-year follow-up shows complete resolution of both GGOs and linearatelectasis (box).
be dismissed. The same applies to patients who experienced ARDS. A strength of our study comes from the choice of excluding participants with these confounding factors, as post-acute COVID-19 lung alterations should be separately considered in these participants. These considerations explain the discrepancy of our data from those of Luger et al (29), who reported that only 69 of 142 participants (49%) with previous COVID-19 pneumonia (including 29% of critically severe patients requiring admission to the intensive care unit) had complete resolution of lung CT abnormalities at 1-year follow-up. Our choice resulted in the selection of participants with moderate lung involvement at disease presentation, thus providing an added value to our findings for future studies. Indeed, it is conceivable that mild to moderate pneumonia will be the most frequent form following widespread vaccination.

We believe that caution should be used to avoid describing residual lung abnormalities as fibrosis at short-term follow-up CT after COVID-19 pneumonia. Efforts should be made to distinguish fibrotic-like abnormalities due to acute inflammatory damage that resolve from slowly progressive fibrosing tissue remodeling that may have a longer course and more subtle evolution. This differentiation is required with the intent to avoid
confusion with reference to terms broadly used with the unique sense of progressive and irreversible fibrosis. Also, such a differentiation has clinical relevance when considering antifibrotic therapies.

Our study has several limitations. First, the study was performed in a single-center setting with a small number of study participants. Second, the temporal changes on CT scans were not matched with symptoms and lung function. Unfortunately, due to severe restrictions aimed at containing the spread of the infection in a hospital setting, lung function procedures were forbidden for much of the study period. Third, noncontrast CT was performed and therefore a combined assessment of pulmonary vasculature was not possible.

In conclusion, our results show that residual lung abnormalities at CT are minimal at 1 year in patients who experienced moderate COVID-19 pneumonia; complete resolution of changes due to COVID-19 pneumonia occurred in 93% of individuals. Confirmation in larger cohorts and the use of new resources like dual-energy chest CT are encouraged to more comprehensively understand the aftermath of SARS-CoV-2 on the lung parenchyma and vasculature.

Author contributions: Guarantors of integrity of entire study, M.B., G.B., E.M., L.C., D.S., G.F., G.R.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, M.B., R.L., E.M., G.B., G.R., L.C., D.S., TV., G.R.; clinical studies, M.B., R.L., E.R., G.S., G.B., E.M., D.S., TV., G.F., G.R.; experimental studies, M.B., G.B., E.M., D.S.; statistical analysis, M.B., G.B., E.M., D.S.; and manuscript editing, M.B., G.B., E.M., D.S., G.R.

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