beneficial for patients with a Pa_{O_2}/FI_{O_2} (P/F) ratio < 150, though many clinicians continue to harbor suspicion that those are not the only patients who benefit. In contrast, trials that enrolled patients regardless of subtype have shown robust mortality benefits. Although studies are urgently needed to examine the hypothesis that Camporota and colleagues articulate, plausibility and internal consistency of a hypothesis are not the standards on which we should base a change in practice. In the particular case of coronavirus disease (COVID-19), we have witnessed the widespread adoption of plausible therapies that subsequently proved to be of no benefit (2). For the present, the best evidence indicates that patients with acute onset of respiratory failure that is not fully explained by fluid overload, bilateral infiltrates, and P/F ratio < 300 on positive-end expiratory pressure (PEEP) of at least 5 cm H_2O benefit from low V_T ventilation, regardless of etiology.

I agree wholeheartedly with the letter writers that lung strain—increment from resting volume—is likely the key mechanical determinant of lung injury in ventilated patients with ARDS. I further agree that V_T alone is a poor proxy for lung strain. There have been signals of this in the literature, notably the retrospective study demonstrating a stronger association of driving pressure with mortality than of V_T (3). It is therefore plausible that there exists a better way to determine what strain is tolerable in a given patient. Absent of evidence, however, we must not become overly persuaded by the plausibility of any given hypothesis. After all, it is very plausible that there exists a way to titrate PEEP to an individual patient's mechanics, and yet, thus far, trials have consistently failed to demonstrate a benefit to individualized PEEP titration.

With respect to their assertion that ARDS secondary to COVID-19 presents with a distinct distribution of respiratory system compliance, the authors are on less solid ground. In support, they cite an editorial by Dr. Marini, which was published in association with an electrical impedance tomography study of 10 patients in a single center. In contrast, the now multiple large case series of patients with COVID-19 (4, 5) report distributions of respiratory system compliance (and P/F ratio) that are remarkably consistent with large case series before the COVID-19 pandemic, such as LUNG-SAFE (Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure) (6). The literature to date simply does not support the idea that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a mechanically distinct form of respiratory failure.

While we await further investigation and potential identification of individualized therapies that improve outcomes, clinicians should feel very comfortable with the continued application of the evidence-based therapies developed in the era before COVID-19. ■

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Are Ground-Glass Opacities on Chest High-Resolution Computed Tomography a Manifestation of Airway Disease?

To the Editor:

We commend the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax for the publication of the first hypersensitivity pneumonitis (HP) clinical practice guidelines (1). The guidelines propose two distinctive subtypes of HP: nonfibrotic and fibrotic, as determined by the presence of radiological and/or histopathological fibrosis.

In their Table 5, the authors propose that a "nonfibrotic typical HP pattern" on chest computed tomography (CT) requires the identification of at least one feature of lung infiltration—mosaic attenuation or ground-glass opacities (GGOs)—plus at least one abnormality indicative of small airway disease—ill-defined centrilobular nodules or air trapping.

However, as the authors pointed out, mosaic attenuation *per se* is not specific for lung infiltration, because in diseases that affect both the lung parenchyma and the small airways (e.g., HP), mosaic attenuation can be due to either GGOs or air trapping and the difference is established by expiratory CT images (1).

Therefore, to be more specific and to avoid confusion, would it not be better to use either GGOs or mosaic attenuation due to GGOs as the sole criterion for lung infiltration on Table 5, because they represent the same phenomenon?

On the other hand, in their Table 6, the authors propose that a "fibrotic typical HP" pattern on CT requires the identification of at least one feature of lung fibrosis in a specific distribution, and at least one abnormality indicative of small airway disease: ill-defined centrilobular nodules and/or GGOs, or mosaic attenuation.

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However, mosaic attenuation is not specific for air trapping, because it can be due to GGOs, particularly in the setting of HP; therefore, to avoid confusion, would it not be better to use either air trapping or mosaic attenuation due to air trapping on expiratory CT images as a criterion for small airway disease?

Finally, in their Table 6 the authors included GGOs as an abnormality indicative of small airway disease in a "fibrotic typical HP" pattern on CT. However, they stated in their Table 4 that GGOs reflect an infiltrative lung disease, which is in agreement with the Fleischner Society, which considers GGOs to be caused by partial filling of airspaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, increased capillary blood volume, or a combination of these (2). We would appreciate clarification of the seemingly contrasting definition of GGOs. ■

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Reply to Morán-Mendoza and Khalil

From the Authors:

We thank Dr. Morán-Mendoza and Dr. Khalil for their important comments regarding the interpretation of high-resolution computed tomography (HRCT) images in nonfibrotic and fibrotic forms of hypersensitivity pneumonitis (HP). We proposed specific combinations of HRCT findings most suggestive of typical HP in Tables 5 and 6, further explained in the text, and clarified the radiological terms used for description of heterogeneous lung attenuation in Table 4 of the guideline document (1). These terms were derived from the Fleischner Society glossary of terms (2).

The points raised by Dr. Morán-Mendoza and Dr. Khalil give us the opportunity to clarify some potential difficulties regarding the descriptions of lung infiltration and ground-glass opacities (GGOs) in HP.

The first point concerns the features of lung infiltration in the typical nonfibrotic HP pattern for which they propose to use either GGOs or mosaic attenuation due to GGOs as the sole criterion for lung infiltration. Whereas we agree that in mosaic attenuation of HP there is a variable degree of infiltration (and thus, GGOs), the most striking feature may be the "hypoattenuated" zones (due to vasoconstriction in the areas of bronchiolitis), seen in the vicinity of lung zones interpreted as having a "normal" attenuation on inspiratory images. This highlights the difficulty of interpreting relative enhancement and/or decrease in attenuation in the lung parenchyma. Because we can observe both aspects in the mosaic attenuation of nonfibrotic HP, we opted to separate the two HRCT findings, reflecting variants in the visual depiction of lung infiltration on HRCT images.

The second point concerns the proposed combination of HRCT features to characterize fibrotic HP. Although there is no apparent concern with the description of HRCT features suggestive of lung fibrosis in HP, questions are raised regarding the HRCT features indicative of small airway disease. Drs. Morán-Mendoza and Khalil interpreted the list as "ill-defined centrilobular nodules and/or GGOs, *or* mosaic attenuation"; however, the intent of the guideline was "ill-defined centrilobular nodules and/or GGOs, *and/or* mosaic attenuation." In fibrotic HP, we listed three features of heterogeneous lung attenuation that could indicate the presence of small airway disease in the background of fibrosis; they are presented from the less specific (i.e., mosaic attenuation) to the most suggestive (i.e., air trapping) HRCT sign, detectable on inspiratory and expiratory images.

The third point deals with the inclusion of GGO in the list of abnormalities indicative of small airway disease in Table 6 of the published document (1). This assumption does not contradict the description proposed by the Fleischner Society as the inflammatory component in HP is located around the bronchioles and also extends into surrounding alveoli; thus, it is responsible for lesions of bronchioloalveolitis. In the context of bronchioloalveolar infiltration, highly profuse centrilobular nodules lead to a uniform ground-glass appearance in the lung parenchyma where both the bronchiolar and alveolar components are mixed. This pathologic-HRCT situation is frequently encountered in clinical practice, for example, in patients with smoking-related abnormalities, and chest radiologists are used to associating extensive GGOs to underlying bronchioloalveolar changes.

We thank Dr. Morán-Mendoza and Dr. Khalil for giving us the opportunity to clarify these different situations with GGOs in HP. ■

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