Reply: COVID-19 Experience and Pulmonary Arterial Hypertension: Do Earlier Theses and New Data Still Match?

From the Authors:

We would like to thank Dr. Segura de la Cal and colleagues for their interest in our work (1) and dedication to these important questions. We share their wish that patients with pulmonary arterial hypertension (PAH) or chronic thromboembolic pulmonary hypertension (CTEPH) might ultimately be found to have a lower-than-expected risk for poor outcomes from coronavirus disease (COVID-19). Nevertheless, we would like to caution against early speculation that pulmonary vascular disease or its treatments may be protective in the setting of COVID-19 infection.

Although case fatality rates for COVID-19 have been hard to estimate (2), overall and age-specific case fatality rates have been reported in the general population of New York and may be reasonable benchmarks (3). The overall case fatality rate in New York was 1.4%. For individuals <64 years old, the case fatality rate was <1%. The case fatality rate then rose dramatically with age. Those aged 65–74 had a case fatality rate of 4.9% and those aged ≥75 had a case fatality rate of 14.2%. We believe these numbers are important to keep in mind when interpreting available data in patients with PAH/CTEPH.

For example, case fatality rates in our United States–based survey (12%) and the international survey of PAH/CTEPH centers (4) (19%) approach or exceed case fatality rates expected for the oldest members of the population (≥75 yr old) in New York. In fact, most patients with COVID-19 in the international survey were <65 years old, making the reported case fatality rate of 19% even more concerning. Dr. Segura de la Cal and colleagues note that their data describing patients with PAH and COVID-19 show an 8% overall case fatality rate. All three deaths (among 39 total cases) were in patients with “significant advanced age.” If we presume that some patients with recognized COVID-19 were <65 years old, the case fatality rate in their older patients must have been over 8% and could possibly be significantly higher depending on the age of the other patients. As such, their data also do not appear to suggest clear protection in the older age group. Published case series include fewer than 100 patients; therefore, we do not yet have sufficient data to suggest or refute the likelihood for protection in younger patients with PAH/CTEPH relative to the general population of the same age (in which case fatality is <1%). Although we acknowledge age-related differences in pulmonary hypertension phenotypes, it seems unlikely that PAH/CTEPH or its treatments would exert a protective effect against COVID-19 in younger patients and a detrimental effect in older patients.

To the broader point, we emphatically agree that these interesting issues are worthy of further study. The respondents are correct to highlight limitations in available population data and to temper any rush to definitive conclusions. Current studies involve small numbers of patients and comparison with the broader population must be done with caution. Differences in confounders, health behaviors, and access to COVID-19 testing (especially early in the pandemic) among patients with PAH/CTEPH might make independent associations of COVID-19 and case fatality either more or less pronounced with respect to the general population than initially reported.

In summary, existing population studies consistently suggest the same or a higher risk for poor outcomes with COVID-19 in patients with PAH/CTEPH relative to the general population. There are deficiencies in available population data, and the results contrast with hypotheses at the bench that may suggest protection (5). We would enthusiastically welcome population data that support better outcomes for these patients; however, barring this evidence, we worry that a premature impression of disease-specific protection might lead some patients with PAH/CTEPH to avoid taking life-saving precautions against contracting COVID-19.

References

1. Lee JD, Burger CD, Delossantos GB, Grinnan D, Ralph DD, Rayner SG, et al. A survey-based estimate of COVID-19 incidence and outcomes among patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension and impact on the process of care. Ann Am Thorac Soc 2020;17:1576–1582.

2. Farha S, Heresi GA. COVID-19 and pulmonary arterial hypertension: early data and many questions. Ann Am Thorac Soc 2020;17:1528–1530.

3. Belge C, Quarck R, Godinas L, Montani D, Escribano Subias P, Vachiéry JL, et al. COVID-19 in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: a reference centre survey. ERU Open Res 2020;6:00520-2020.

4. Nuche J, Pérez-Olivares C, Segura de la Cal T, Jiménez López-Guarch C, Arribas Ynsaurriaga F, Escribano Subias P. Clinical course of COVID-19 in pulmonary arterial hypertension patients. Rev Esp Cardiol (Engl Ed) 2020;73:775–778.

5. Segura de la Cal T, Nuche J, Jiménez López-Guarch C, Pérez-Olivares C, Velázquez M, López-Medrano F, et al. Unexpected favourable course of coronavirus disease 2019 in chronic thromboembolic pulmonary hypertension patients. Arch Bronconeumol 2020;56:749–752.

6. Nuche J, Segura de la Cal T, Jiménez López Guarch C, López-Medrano F, Delgado CP-O, Ynsaurriaga FA, et al. Effect of coronavirus disease 2019 in pulmonary circulation: the particular scenario of precapillary pulmonary hypertension. Diagnostics (Basel) 2020;10:548.

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A Role for Steroids in COVID-19–associated Pneumonitis at Six-Week Follow-Up?

To the Editor:

We read with interest the recent paper by West and colleagues (1) regarding the use of corticosteroids in persistent inflammatory interstitial lung disease (ILD) after a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. In their timely and well-implemented observational treatment study, 3.6% of patients with coronavirus disease (COVID-19) discharged from the hospital were diagnosed with persisting organizing pneumonia at 6 weeks and deemed eligible for corticosteroid treatment. Cases were assessed in a multidisciplinary team meeting, and lung function was performed before and after treatment.

As ILD physicians in a tertiary referral center, we have extensive experience in treating organizing pneumonia with corticosteroids in the context of autoimmune disease, adverse drug reactions, and infection. We agree that, intuitively, corticosteroids should have a role in the treatment of patients with significant parenchymal disease secondary to COVID-19. From our own large cohort captured during a similar time frame, before acute corticosteroid treatment was the standard of care (2, 3), the incidence of interstitial changes at 6-week follow-up is comparable to these data. However, in our cohort without targeted outpatient corticosteroid administration, there was a significant spontaneous recovery in the majority of patients by 12 weeks. This raises the question as to whether there would have been some spontaneous recovery in these patients without any intervention, especially as there is no matched comparator group. Treatment was only offered if patients were not getting better on a weekly basis, but it is not clear how this assessment was made. It is also important to note that, although treatment was for a short duration, these patients had obesity (25.7%), hypertension (31.4%), and diabetes (22.9%) and were therefore a population in which steroids would ideally be avoided if possible.

We applaud the speed and completeness of this work, particularly in the current climate when access to aerosol-generating respiratory physiology testing to robustly quantify changes is challenging. However, there is clearly equipoise about the use and timing of corticosteroid administration and how they affect the natural history of COVID-19 associated with organizing pneumonia. The RECOVERY (Randomized Evaluation of COVID-19 Therapy) trial (2) showed that dexamethasone resulted in reduced 28-day mortality in those patients requiring oxygen and is now standard of care. The natural history of COVID-19 associated with organizing pneumonia and impact on the process of care. Ann Am Thorac Soc 2020;17: 1576–1582.

References

1. Lee JD, Burger CD, Delossantos GB, Grinnan D, Ralph DD, Rayner SG, et al. A survey-based estimate of COVID-19 incidence and outcomes among patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension and impact on the process of care. Ann Am Thorac Soc 2020;17: 1576–1582.

2. Rajgor DD, Lee MH, Archuleta S, Bagdasarian N, Quek SC. The many estimates of the COVID-19 case fatality rate. Lancet Infect Dis 2020;20:776–777.

3. Yang W, Kandula S, Huynh M, Greene SK, Van Wye G, Li W, et al. Estimating the infection-fatality risk of SARS-CoV-2 in New York City during the spring 2020 pandemic wave: a model-based analysis. Lancet Infect Dis 2021;21:203–212.

4. Belge C, Quarc R, Godinas L, Montani D, Escribano Subias P, Vachiéry JL, et al. COVID-19 in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: a reference centre survey. EPU Open Res 2020;6:00520-2020.

5. Farha S, Heresi GA. COVID-19 and pulmonary arterial hypertension: early data and many questions. Ann Am Thorac Soc 2020;17: 1528–1530.

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