

Letter to the Editor regarding “Could pulmonary arterial hypertension patients be at lower risk from severe COVID-19?”

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It was with great interest and some concern we read the recently published paper “Could pulmonary arterial hypertension (PAH) patients be at lower risk from severe COVID-19.”¹ In this paper, the authors quote an electronic survey of the Pulmonary Hypertension Association (PHA) centers conducted in March 2020, which only yielded 13 confirmed cases of COVID-19 in known PAH patients. Based on these results, they speculate that PAH patients may have an attenuated COVID-19 course due to potential protective features of PAH-targeted therapies (endothelin receptor antagonists, phosphodiesterase type 5 inhibitor (PDE) inhibitors or prostanoids). We are concerned about the possible detrimental effects misinterpretation of this message could have to the PAH community. These assumptions were based on little data at an early stage of the pandemic in the US, and the resulting speculations could mislead and put PAH patients at higher risk. SARS-CoV2 and its related illness can have devastating effects on those with pre-existing medical conditions including PAH, and assuming protective effects of their medical therapy may lead PAH patients to altering their behavior by providing a false sense of security.

A closer look at the data that was presented underscores that PAH patients are not at lower risk for severe COVID-19 and may even carry a risk for more severe illness. The authors’ methodology of collecting survey results is subject to response bias as it is unclear how many centers responded and how many PAH patients were included to find the 13 COVID-19 positive patients. Additionally, this survey was conducted at a time in March when many centers were constrained in their ability to test patients with symptoms of COVID-19 and the US was only at the beginning of the disease acceleration. Some speculate that the number of COVID-19 cases identified may only represent a fraction of the total infections circulating.² As serologic tests become widely available, we hope to better approximate

the total number of infections including those with mild or no symptoms.

Furthermore, based on the data presented in the paper, 53.8% of the patients with PAH and COVID-19 required hospitalization, 23.1% required intubation and 7.7% died. Compared to the early data from China, these estimates are actually higher in this report of PAH patients than what was observed in the general population in Wuhan (2.3% of all laboratory confirmed cases required intubation and case-fatality rate was 1.4%).³ In comparison, reports from Italy note 5.0% of all patients having critical illness with a 7.2% case-fatality rate.⁴ Moreover, in this very limited sample of PAH patients, there are large error bars around the estimates and there is little to no evidence supporting the speculation that PAH patients could be protected from COVID-19.

Although the authors provide speculation into the downstream effects of various PAH medications which may be protective against Acute respiratory distress syndrome (ARDS), they did not mention potential harms. A significant concern with the use of PAH-targeted therapies in patients with severe COVID-19-associated ARDS is the potential for worsening ventilation/perfusion (V/Q) matching and obliterating the hypoxemic vasoconstrictive response to areas of infiltrated lung parenchyma, as was seen with the use of sildenafil in patients with COPD-associated pulmonary hypertension.⁵ In PAH patients with COVID-19 infection, worsening hypoxemia has potential for real harm as many with severe hypoxemia will require intubation.

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In conclusion, although this is clearly a time that some speculation and assumptions are important to pose better questions, advance knowledge and push COVID-19-related research forward, we must be careful not to confuse this with over-reaching conclusions. The language we use and the uncontrolled, retrospective data we present in the literature can be misconstrued and have the opposite effects of what was expected. In the era of social media and massive dissemination of information, opinions, assumptions and speculation (even admitted by the authors in this case) if not presented appropriately have serious potential for harm. There is potential for this information to be misunderstood by a lay patient as to mean PAH patients can be reassured of a lower risk for severe COVID-19 than the general population. Such an interpretation may result in less stringent social distancing or hand hygiene practices. The unified message from all PAH providers should be that there is little data on the effects of PAH or related therapies on COVID-19 and until we have such data, all efforts should be focused on avoiding infection through social distancing and good hygiene.

Conflict of interest

The author(s) declare that there is no conflict of interest.

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