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Spontaneous Pneumothorax (SP) in COVID-19 Is Associated With Worse Outcomes Than SP in Non-COVID-19 Patients, Which Suggests That SP in COVID-19 is a Sign of Disease Severity



Is This Finding a Pure Association or Is There Really a Strong Relationship Between the Two?

To the Editor:

We read with great interest the recent article in *CHEST* (March 2021) by Miró et al¹ who concluded that spontaneous pneumothorax (SP) is associated with worse outcomes than SP in patients without COVID-19 and in patients with COVID-19 without SP. We would like to comment. When we look carefully to the results, we see that 32.3% of the patients with COVID-19 with SP went to ICU and that patients died significantly more with an OR of 4.07.¹ Compared with the control group that did not have COVID-19 with SP, the ICU admission was only 2.6%, and the mortality rate was 1.6%. Compared now with COVID-19 without SP, ICU admission was only 1.8%, and the mortality rate was 13.8%.¹ Clearly, the two control groups were much less sick when we see the ICU admission compared with COVID-19 with SP. So, there is no certainty that SP is a sign of higher severity on itself because it might be just a pure association and not a strong relationship. Indeed, the difference in severity might be due to other comorbidities not described in the study. The literature is very controversial regarding the mortality rate and this potential relationship. In a study looking at 15 cases of COVID-19, spontaneous pneumomediastinum was associated with a much lower mortality rate of 26%.² In another cohort study

with 18 patients with SP, the mortality rate was only 27%.³ In another review, the authors concluded that it should be emphasized that a causal relationship between COVID-19 severity and pneumothorax cannot be concluded.⁴ The presence of prior bullous disease, underlying connective tissue disease, hormonal irregularities, environmental exposure, and vigorousness of coughing are unknown considerations.⁴ The majority of these precipitating factors were not evaluated in the study of Miro et al.¹ In addition, when comparing COVID-19 with SP with COVID without SP, we found that history of asthma was significantly higher (20% vs 6.8%) as was dyspnea (87.5% vs 54.3%), which are well-known precipitating factors for SP. Regarding the severity of the disease between COVID-19 with SP compared with COVID-19 without SP, classic severity indicators for COVID-19 were not different between the two groups, such as C-reactive protein levels, procalcitonin levels, and aspartate amino transferase levels.¹ In a more recent study,⁵ the authors showed the importance early surgical treatment for SP, and we do not know how many of the patients in the study of Miro et al¹ underwent rapid surgery that could save their lives.

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Response



To the Editor:

We would like to provide responses to the comments by Honore et al in relation to our recent report on spontaneous pneumothorax (SP) in patients with COVID-19.¹

First, we absolutely agree that, despite the higher mortality rate observed in our cases with respect to control subjects, our report does not preclude any pathophysiologic relationship between COVID-19 and SP, because the latter could just be an additional sign of COVID-19 severity. In fact, due to the limited number of cases, we adjusted mortality rates only for age, sex, and center, but not for comorbidities or disease severity. As Honore et al underline, cases were sicker than control subjects, as suggested by the higher rate of ICU admission and by the fact that patients with COVID-19 and SP more frequently had asthma (as a comorbidity) and dyspnea (as the main complaint) than patients with COVID-19 without SP, which could explain by itself our reported higher mortality rate.

Second, they claim our mortality rate is higher than the mortality rate that they calculated according to two papers that reviewed previous literature.^{2,3} In the absence of a clear, extensive, and well-designed search strategy, these revisions could provide inaccurate estimations. For example, readers must be aware that these two reviews included several identical patients and that a careful analysis renders only 26 unique cases, with five patients (19.2%) dying during the episode. This mortality rate is not statistically different from that reported in our series (13 deaths in 40 patients; 32.5%; $P = .24$). Furthermore, some cases in these reviews received noninvasive ventilation and could not correspond to real SP. Therefore, we believe that our unique study with a predefined methods for patient inclusion at ED arrival (before any noninvasive ventilation was initiated) that was included within a grand multicenter project to identify unusual manifestations of COVID-19^{4,5} provides a more

reliable approach to mortality rates in patients with COVID-19 who are experiencing the development of SP.

Third, although we acknowledge that we did not record prior bullous disease, underlying connective tissue disease, hormonal irregularities, environmental exposure (with the exception of tobacco), and vigorosity of coughing, most of these factors are difficult to measure, and neither have they been evaluated in previous reports of SP in patients with COVID-19.

And last, Honore et al ask how many of our patients underwent rapid surgery. As stated in our original report, a thoracic tube was placed in 29 of the 40 patients (72.5%) to relieve pneumothorax, which is a significantly higher percentage than that observed in patients included in aforementioned reviews (11 of 26 patients; 42.3%; $P = .01$). This provides additional evidence that our patients were really sick and makes it unlikely that the lack of SP treatment could have influenced our reported high mortality rate, as our colleagues seem to suggest.

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