confirmed by cardiac catheterization with increased pulmonary vascular resistance and decreased cardiac index (1). Of the 14 patients with precapillary PH with increased PAWP diagnosed during hemodynamic follow-up, 3 patients died during hospitalization for COVID-19, representing a mortality rate of 21.4% that is in accordance with the overall mortality of the entire cohort (24.6%; 95% confidence interval, 18.8–30.5%). It is likely that some patients with precapillary PH had associated heart failure with preserved ejection fraction (HFpEF), as evidenced by the occurrence of increased PAWP in a subset of patients undergoing hemodynamic monitoring. However, the increase in PAWP in patients with precapillary PH was not associated with excess mortality in our cohort. It is nevertheless likely that HFpEF was probably underestimated in patients with precapillary PH, as fluid challenge was not systematically performed during right cardiac catheterization to diagnose HFpEF.

Similarly, the D_{LCO} of 53.5% (95% confidence interval, 35–66%) reported in our cohort is in accordance with the etiologies of precapillary PH, including mainly PAH and chronic thromboembolic PH but also pulmonary venoocclusive disease and chronic respiratory disease–associated PH, which are all typically associated with major decreases in D_{LCO}. Indeed, Hoeper and colleagues recently reported that low D_{LCO} (<45%) was frequently observed in patients with diagnoses of idiopathic PAH, and this may represent a specific phenotype close to group 3 PH (6). In our cohort, we observed an increased risk of mortality in patients with chronic respiratory diseases, giving an obvious explanation for the lower D_{LCO} in deceased patients. The recent 2022 European Society of Cardiology/European Respiratory Society guidelines highlight that comorbidities, including decrease in D_{LCO}, were associated with worse response to PAH-approved drugs in patients with PAH (7).

In conclusion, the prevalence of cardiovascular and pulmonary comorbidities reported in our cohort is in accordance with the epidemiology of patients with precapillary PH in large national registries. Although it is possible that some patients had occult HFpEF, a small number had elevated PAWP during follow-up, and this was not associated with outcomes. Univariate and multivariate models demonstrated significant associations between chronic respiratory and cardiovascular diseases and the risk of in-hospital mortality in patients with precapillary PH. This is not surprising given that cardiopulmonary comorbidities are considered poor prognostic factors for PH and COVID-19. ■

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David Montani*
Université Paris-Saclay
Le Kremlin-Bicêtre, France

Hôpital Marie Lannelongue
Le Plessis Robinson, France

and

Hôpital Bicêtre
Le Kremlin-Bicêtre, France

Jason Weatherald
University of Calgary
Calgary, Alberta, Canada

Marc Humbert
Olivier Sitbon
Université Paris-Saclay
Le Kremlin-Bicêtre, France

Hôpital Marie Lannelongue
Le Plessis Robinson, France

and

Hôpital Bicêtre
Le Kremlin-Bicêtre, France

ORCID IDs: 0000-0002-9358-6922 (D.M.); 0000-0002-0615-4575 (J.W.); 0000-0003-0703-2892 (M.H.); 0000-0002-1942-1951 (O.S.).

*Corresponding author (e-mail: david.montani@aphp.fr).

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Resolving the Microbial Burden with Tailored Immune Modulation in COVID-19 Acute Respiratory Distress Syndrome?

To the Editor:

Nonresolving acute respiratory distress syndrome (ARDS) with prolonged mechanical ventilation has been common during the previous severe acute respiratory syndrome coronavirus 2

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(SARS-CoV-2) outbreaks and has had markedly high mortality (1). Therefore, we read with great interest in a recent issue of the *Journal* the study by Kullberg and colleagues describing the potential role of lung microbiota in nonresolving coronavirus disease (COVID-19)-associated ARDS (2). In this observational cohort study, regularly collected BAL fluids from mechanically ventilated patients with COVID-19 were analyzed for bacteria and fungi using the 16S sequencing technique and related to outcome. We would like to raise three points.

First, the authors reported at the group level that an increased bacterial and fungal load led to a prolonged duration of mechanical ventilation, higher mortality, and more microbiotic dysbiosis such as pneumonia and COVID-19–associated pulmonary aspergillosis. In addition, this microbiotic load was also associated with an increased inflammatory response. Unfortunately, the authors failed to discriminate the patients with a low or high proinflammatory response related to the microbiological burden. This could have played an important role in the outcomes reported. Second, at an individual level, the initial load of bacteria and fungi was insufficiently distinctive for daily clinical practice. Not to mention that 16s sequencing is (not yet) available in all hospital laboratories. Third, the application of selective decontamination of the digestive tract is supposed to be routine care in the Netherlands according to Dutch guidelines (3). However, the results indicate a persistent carrier state of gram-negative bacteria, which is surprising and worrying at the same time.

The authors are to be congratulated on this scientific approach to a relevant clinical problem. But how may we translate this observational study into our daily practice? The strict monitoring of infections, including COVID-19–associated pulmonary aspergillosis in COVID-19–associated ARDS, is correctly stressed, given that early recognition and timely treatment likely improves the patient outcome (4). In addition, the importance of recognition and suppression of a secondary immunological disorder, whether or not caused by a low-grade infection, cannot be emphasized enough (5). Hopefully, the techniques used in this study will enable early diagnosis and treatment of pulmonary infections in the foreseeable future. Until then, we probably need additional approaches, including selective decontamination of the digestive tract and patient-tailored immune modulation to further improve outcomes in COVID-19–associated ARDS. ■

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Marnix Kuindersma, M.D.*
Department of Intensive Care Medicine
Gelre Hospitals
Apeldoorn, the Netherlands

Peter E. Spronk, M.D., Ph.D.
Department of Intensive Care Medicine
Gelre Hospitals
Apeldoorn, the Netherlands

and

Expertise Center for Intensive Care Rehabilitation Apeldoorn
Apeldoorn, the Netherlands

*Corresponding author (e-mail: m.kuindersma@gelre.nl).

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Efficacy of High-Flow Nasal Cannula Oxygen Therapy in Reducing Future Exacerbations for Patients with Stable Hypercapnia with Chronic Obstructive Pulmonary Disease

To the Editor:

We have read with great interest the article by Nagata and colleagues (1) published in this issue of the *Journal*, "Home High-Flow Nasal Cannula Oxygen Therapy for Stable Hypercapnic COPD: A Randomized Trial," which provided positive results for long-term high-flow nasal cannula oxygen therapy (HFNC) in reducing the risk of moderate/severe exacerbations in patients with stable hypercapnia and chronic obstructive pulmonary disease (COPD). We congratulate Nagata and colleagues for this excellent work that provides more choices for this population. Compared with previously published studies, several advancements, such as controlling the adherence to HFNC and recruiting only patients with hypercapnia, have been made in their work. Nevertheless, the study has some flaws that deserve more discussion.

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