Monitoring Fractional Exhaled Nitric Oxide Levels in Adult Patients With Acute Symptomatic COVID-19 Infection: Non Sequitur?

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To the Editor:

We read with interest the recent article by Betancor et al [1] published in the Journal. The authors found that fractional exhaled nitric oxide (FeNO) levels in 82 patients with acute symptomatic SARS-CoV-2 infection (COVID-19) were within the normal range.

Current concepts suggest that local elaboration of nitric oxide (NO) modulates, in part, the intense proinflammatory phenomena observed in the lungs of patients with certain respiratory viral infections [2]. To that end, FeNO monitoring is proposed as simple, portable, noninvasive, cost-effective, point-of-care, and rapid biomarker of pulmonary inflammation in patients with virus-induced acute lung injury [2]. However, the reported effects of acute symptomatic COVID-19 infection on FeNO levels in humans are controversial. Exline et al [3] reported significantly higher FeNO levels in 23 hospitalized, mechanically ventilated patients with acute COVID-19 infection than in controls. Likewise, Balci et al [4] and Yang et al [5] found significantly higher FeNO levels in patients with acute symptomatic COVID-19 infection than in controls. By contrast, Lior et al [6] showed recently that FeNO levels are significantly decreased in 56 hospitalized patients with severe COVID-19 infection and that FeNO <11.8 ppb portends adverse outcomes. Taken together, these studies suggest that in patients with acute symptomatic COVID-19 infection, FeNO is not a useful biomarker for monitoring disease outcomes.

The reason(s) underlying these discrepant results are uncertain. Conceivably, differences in patient characteristics, such as age, sex, race/ethnicity, smoking history, disease severity, and therapeutic interventions at the time of FeNO testing, could have accounted, in part, for these discordant

observations [1,3-6]. For instance, prolonged normobaric hypoxia has been shown to increase FeNO levels, while short-term hyperoxia decreases FeNO levels for several hours [7-9]. To the best of our knowledge, the effects of normobaric hypoxia and hyperoxia on FeNO levels in patients with acute symptomatic COVID-19 infection have not been reported to date. In addition, Betancor et al [1] found that treatment of hospitalized patients with COVID-19 infection with corticosteroids was associated with a significant decrease in FeNO levels.

A major limitation of these studies is their small sample size. Accordingly, larger, prospective studies are warranted to address the clinical utility of point-of-care FeNO monitoring in patients with acute symptomatic COVID-19 infection to inform short- and long-term outcomes.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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