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Reply to Modesto-Alapont *et al.*

From the Author:

I thank Dr. Modesto-Alapont and colleagues for their thoughtful comments on my editorial (1). They state that mechanical ventilation is ideally instituted on the basis of precise diagnosis and cite one of my chapters. The chapter says the exact opposite. Indeed, they quote a sentence in which Dr. Laghi and I say that physicians do not initiate mechanical ventilation consequent to “slotting a patient into a particular diagnostic pigeonhole.” (2)

Dr. Modesto-Alapont and colleagues claim that the Berlin definition enhances the ability to make a precise diagnosis of acute respiratory distress syndrome (ARDS) in patients with coronavirus disease (COVID-19). On the contrary, the question of whether patients with COVID-19 have typical ARDS (or not) is presently much debated. But there is a deeper question. Criteria used in formulating all definitions of ARDS (over the past 32 years) have been chosen arbitrarily with the goal of setting tight boundaries to achieve greater uniformity of patients entered into clinical research studies. None of the definitions of ARDS constitute, in nosological terminology, a “natural kind” (3) on a clinical, etiologic, or even a physiological level. If $\text{PaO}_2/\text{FiO}_2$ is 299 on positive end-expiratory pressure 6, the patient has ARDS by the Berlin definition. If, 5 minutes later, body posture is altered and $\text{PaO}_2/\text{FiO}_2$ increases to 301, the patient no longer has ARDS. It is imperative that explicit criteria be followed meticulously when entering patients into clinical trials. A wise clinician, however, would believe it daft to switch between diagnostic categories on the basis of a 2-unit difference on a single laboratory test.

Leaving aside the arbitrary nature of ARDS criteria, the diagnosis does not provide justification for a fixed course of action (other than avoiding a V_T of 12 ml/kg). Some patients with ARDS undergo invasive mechanical ventilation, whereas others are sustained with high levels of supplemental oxygen or noninvasive ventilation without ever being intubated (4, 5).

Dr. Modesto-Alapont and colleagues discuss the role of hypothesis and refutation in science. Although they do not state their hypothesis explicitly, it would appear to be along the lines that instituting mechanical ventilation on the basis of a physician's gestalt versus a precise diagnosis results in inferior clinical outcome. They claim that the results of the randomized control trial by the REVA Research Network have tested (and refuted) that hypothesis. Leaving aside that the hypothesis does not possess the

characteristics of a good hypothesis (6), especially in terms of parsimony, the data of the REVA trial cannot be used to refute or accept the hypothesis. The focus of the REVA trial was the target for oxygenation during the entire course of mechanical ventilation subsequent to intubation. The results of the REVA trial do not relate to the decision of whether (or not) to intubate a patient. Drawing a parallel between the two is to conflate fundamentally different situations. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Are Patients with COVID-19 Dying or with Cardiac Injury?

To the Editor:

We read with great interest the paper by Du and colleagues presenting the clinical characteristics of 85 patients in Wuhan dying of coronavirus disease (COVID-19) (1). Around 70% presented

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