[General Interest Commentary and Announcement]

CHEST

Does Making a Diagnosis of ARDS in Patients With Coronavirus Disease 2019 Matter?

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The question "Do patients with coronavirus disease 2019 (COVID-19) develop typical ARDS?" is arousing fevered debate. Respondents pivot their answers around the nature of COVID-19, rather than ARDS. The controversy unveils riddles at the core of ARDS. What exactly is ARDS, and how should a doctor decide whether some patient has ARDS or another disorder?

In the founding report, Ashbaugh et al[1] christened the new disorder a "syndrome" because it encompassed a grouping of clinical and pathophysiologic abnormalities with no known cause. After its baptism, its very existence was called into question. Dr Fishman, editor of the first multivolume textbook of pulmonary medicine, denigrated it a "distinctive non-entity."[2]

Another critic remonstrated that making a diagnosis of "ARDS is not helpful because it obscures a clinically very important differential diagnosis."[3] That grumbler was Dr Murray,[3] who later enumerated a scoring system to adjudge whether a patient has ARDS. Dr Murray never explained his volte-face in resurrecting a syndrome he had previously tried to terminate (rest in peace).

Subsequent panels (the American-European Consensus Committee and the Berlin panel) rearticulated criteria for defining ARDS. Designated criteria were chosen with a goal of setting tight boundaries to achieve greater uniformity of patients who were being enrolled in clinical trials. Each new formulation was justified by specifying grave flaws in its predecessor. None of the redefinitions represented a radical change from the initial description of Ashbaugh et al.[1]

The Berlin definition claims that ARDS can be diagnosed only if onset is within 7 days of a known insult. Observing that respiratory failure occurred 8 to 12 days after first symptoms of COVID-19 in Chinese series, Li and Ma[4] concluded that these patients should not be diagnosed with ARDS. Other commentators consider high compliance measurements as grounds for doubting typical ARDS in patients with COVID-19.

The claims and counterclaims fail to acknowledge that ARDS is a man-made creation. Contrast ARDS with measles, which is caused by a nonredundant etiologic agent (virus), with uniform pathogenesis and a rash so characteristic that diagnosis is self-evident. Nosologically, measles constitutes a "natural kind" on etiologic, pathogenetic, and clinical levels. ARDS does not represent a natural kind on any level.

Each constituent in ARDS definitions has fuzzy boundaries. Hypoxemia is identified by Pao_2/Fio_2. In patients with ARDS with fixed shunt, alterations in Fio_2 caused Pao_2/Fio_2 to fluctuate unpredictably by >100 mm Hg.[5] In patients who fulfill all ARDS criteria, administration of 100% oxygen for 30 minutes caused Pao_2/Fio_2 to increase such that 58.5% were no longer categorized as ARDS.[6]

When ARDS-Network researchers interpreted chest radiographs according to American-European Consensus Committee criteria, agreement was only moderate (kappa = 0.55) with full agreement on less than one-half of the radiographs.[7] This poor performance was one justification for the development of the Berlin definition. Subsequent evaluation of the Berlin criteria

ABBREVIATIONS: COVID 19 = coronavirus disease 2019; PEEP = positive end-expiratory pressure

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found interobserver agreement no better (kappa = 0.50), with 67% disagreeing on imaging interpretation.[8]

Too much attention is focused on the definition of ARDS. Placing it on an altar for veneration is unwarranted. Getting pedantic as to whether a patient with COVID-19 truly satisfies criteria for ARDS is a distraction from patient care. Definitions beget a sense of finality (often unjustified) and can confine the mind rather than liberate it.

Few diagnoses dictate an invariant course of action. Diagnosing pneumothorax is not inevitably followed by needle drainage; high concentration of oxygen is preferable in certain circumstances. All patients with ARDS do not require intubation; some are sustained with supplemental oxygen or noninvasive ventilation. A central criticism of ARDS is its heterogeneity; a diagnosis of ARDS may halt the search for the underlying cause.[9] This criticism does not apply to respiratory failure in patients with COVID-19: we know that it is caused by severe acute respiratory syndrome coronavirus 2 and that no therapy is effective against the virus.

The only consequent of ARDS diagnosis is avoiding tidal volume 12 mL/kg. Given that tidal volume 12 mL/kg is not used in any patient, making a diagnosis of ARDS does not impact selection of any ventilator setting. Tidal volume 6 mL/kg has not been proved superior to tidal volume 11 mL/kg (or anything in between), nor is 6 mL/kg appropriate in every patient. Decrements in tidal volume are accompanied necessarily by shortening of mechanical inspiratory time. Once mechanical inspiratory time becomes less than the patient's neural inspiratory time, double triggering is inevitable.[10] A doctor may set tidal volume 6 mL/kg, but the patient is receiving 12 mL/kg.

Treating patients with ARDS according to the ARDS-Network PEEP-F_{IO_2} table is especially mindless. At F_{IO_2} 60%, the patient gets either positive end-expiratory pressure (PEEP) 10 or 20 cm H_2O, no other options. At F_{IO_2} 80%, the patient gets either PEEP 14 or 22 cm H_2O. Neuromuscular-blocking agents decreased ARDS mortality rate in one study but were without benefit in a subsequent trial. Effect of prone positioning on ARDS death has been variable.

The identification of phenotypes and endotypes arouses much interest, but this is still (sub)group thinking. Searching for subgroups is apposite for research investigations but not applicable for individualized care.

The mindset for care at the bedside is antithetical to that needed for conducting clinical trials. Each patient is unique; even twins from the same ovum are different.

Respiratory physiology in patients who are undergoing mechanical ventilation is complex. It is impossible to predict the net response of multiple counterbalancing reflex pathways that are incited by a single alteration in a ventilator setting. There is no substitute for making changes and observing the effect on plateau pressure, airway pressure waveform, double triggering, Pa_{O_2}, BP, and so on[10] and then iteratively fine-tuning the settings.

Based on personal experience of teaching residents at the bedside for more than four decades, the cognitive task that trainees find most challenging is to separate wheat from chaff, to ward off distractions in a complex case and identify the pivotal factor that will decide a patient's outcome. For the doctor at the bedside of a patient with COVID-19, making a diagnosis of ARDS is completely irrelevant. No clinical action will follow directly from the diagnosis. The debate presently raging as to whether COVID-19 produces typical or atypical ARDS is an unfortunate distraction from the central questions that decides a patient's outcome.

The cognitive challenges in COVID-19 revolve around interpretation of blood oxygen levels[11,12] and deciding whether to insert an endotracheal tube.[13] It is a tragedy to think that some patients with COVID-19 were intubated simply because oxygen was being delivered at >6 liters/min targeted to a nonscientific pulse oximetry objective.

We tend to forget that diseases have no separate existence independent of patients. As doctors we treat patients, not diseases. Management requires customized care that is tailored to each patient's unique physiologic response, not mindlessly following a protocol assembled for an ARDS cookbook.

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References

1. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. *Lancet*. 1967;2(7511):319-323.
2. Fishman AP. Shock lung: a distinctive nonentity. *Circulation*. 1973;47(5):921-923.
3. Murray JF. Editorial: the adult respiratory distress syndrome (may it rest in peace). *Am Rev Respir Dis*. 1975;111(6):716-718.
4. Li X, Ma X. Acute respiratory failure in COVID-19: is it "typical" ARDS? *Crit Care*. 2020;24(1):198.

5. Gowda MS, Klocke RA. Variability of indices of hypoxemia in adult respiratory distress syndrome. *Crit Care Med*. 1997;25(1):41-45.

6. Ferguson ND, Kacmarek RM, Chiche JD, et al. Screening of ARDS patients using standardized ventilator settings: influence on enrollment in a clinical trial. *Intensive Care Med*. 2004;30(6):1111-1116.

7. Rubenfeld GD, Caldwell E, Granton J, Hudson LD, Matthay MA. Interobserver variability in applying a radiographic definition for ARDS. *Chest*. 1999;116(5):1347-1353.

8. Sjoding MW, Hofer TP, Co I, Courey A, Cooke CR, Iwashyna TJ. Interobserver reliability of the Berlin ARDS definition and strategies to improve the reliability of ARDS diagnosis. *Chest*. 2018;153(2):361-367.

9. Vincent JL, Santacruz C. Do we need ARDS? *Intensive Care Med*. 2016;42(2):282-283.

10. Tobin MJ, Jubran A, Laghi F. Fighting the ventilator. In: Tobin MJ, ed. *Principles and Practice of Mechanical Ventilation*. 3 ed. New York: McGraw-Hill Inc; 2012:1237-1258.

11. Tobin MJ. Basing respiratory management of COVID-19 on physiological principles. *Am J Respir Crit Care Med*. 2020;201(11):1319-1320.

12. Tobin MJ, Laghi F, Jubran A. Why COVID-19 silent hypoxemia is baffling to physicians. *Am J Respir Crit Care Med*. 2020;202(3):356-360.

13. Tobin MJ, Laghi F, Jubran A. Caution about early intubation and mechanical ventilation in COVID-19. *Ann Intensive Care*. 2020;10(1):78.