The First Day in ARDS Care: Your First Steps Should Be Your Best

As we care for patients with ARDS, we aim to provide the best evidence-based care. Studies and guidelines that provide best practices abound. The mortality ascribed to ARDS, however, remains elevated. Yet, adoption of these best practices has not occurred at the pace we would desire.[1] In a retrospective cohort that spans almost 2 decades, Kallet et al[2] present an in-depth analysis of a cohort of subjects with ARDS who were admitted to the ICUs of San Francisco General Hospital (an ARDSNet study site). This is a unique cohort, in which patients were screened daily and classified based on the inclusion and exclusion criteria for the lower tidal volume trial from ARDSNet.[3] This study provides a view into the epidemiologic aspects of this population and, perhaps more importantly, into the processes of care applied for subjects with ARDS who were screened but not enrolled (eligible and ineligible) for randomized controlled trials.

Kallet et al[2] delve into a nuanced discussion to generate a deeper understanding about the observed higher mortality in observational studies of subjects with ARDS. As has been argued before, patients who were not eligible for an ARDS clinical trial were sicker, with higher severity of illness scores, more co-morbidities, and a higher mortality than patients eligible for clinical trials.[4] There were marked differences between patients who were eligible and those who were not eligible in the etiology of ARDS, location of care, and singular comorbidities (eg, traumatic brain injury, moribund). These underlying conditions independently affected the outcomes in the study cohort and highlight the folly of comparing outcomes of observational trials with those of randomized control trials. The current study shows that, across time, these populations were dramatically different, and, as a result, one can argue that the non-eligible population is more vulnerable, and, thus, that the implementation of best care practices and consistent care is even more important for these patients.

Kallet et al,[2] within the acknowledged limitations of their cohort, were able to describe the effects of exposure to protocolized care and best practices on outcomes. The subjects who received protocolized lung-protective ventilation

SEE THE ORIGINAL STUDY ON PAGE 1380

had a lower mortality compared with the subjects who did not receive this care. The authors need to be commended that a high proportion of subjects with ARDS in their cohort received protocolized care. What were the factors that led to this? Perhaps the most evident to us was that the ICUs had a process in place to screen all patients admitted within the first 24 h, and, thus, recognized early subjects with ARDS. Although not all received protocolized care, the majority had consistent plateau pressure measurements and received lung-protective ventilation. A remarkable achievement when compared with the reported literature, and a testament to the center's investment in respiratory therapy education and systematic ARDS care.[1] Clearly, early recognition of a syndromic disease as complex and varied as ARDS increases the chances of receiving appropriate therapy. Although the influence of early interventions based of clinical parameters and their subsequent consequences on outcomes may not be clinically intuitive up front, this has a downstream impact, and most predictive models operate under this paradigm.[5] In our opinion, the study by Kallet et al[2] shows that the early recognition of a disease, ICU care in the first 24 h, and the institution of appropriate ventilator therapy and monitoring had a cascading impact on the eventual outcomes in subjects who were critically ill. Early identification of patients at risk of ARDS or those with ARDS on admission initiates a series of clinical and therapeutic responses that have quantifiable consequences downstream. Disease identification helps the team focus on tailored management of the patient. It would be harder to permit injurious ventilation when the clinician is aware that the patient has ARDS.

In this cohort, the subjects in whom a protocol was not followed had worse outcomes, even when achieving lung-protective goals. Why did clinicians choose not to use the protocol? The severity of disease (eg, too ill), comorbidities (eg, COPD), the environment of care (eg, new personnel or new policies), or evidence uncertainty (eg, evidence changes or controversies) are some of the potential causes. A well-intentioned deviation from established practices that results from clinical compulsions (perceived or actual) encountered by the physician and personal biases for or

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Correspondence: Eduardo Mireles-Cabodevila MD. E-mail: mirelee@ccf.org.

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against a certain therapy as a cofactor cannot be discounted and are not without its clinical consequences. We suspect that, even though the initial settings were appropriate (demonstrating clinician knowledge and spirit of lung protection), once the path was set outside the protocol, the patients who received clinician-driven care may lack clear instructions (to the rest of the team, the rest of the time), which led to inconsistent care. Recognition, explicit protocols, and systematic application are the only ways to generate actionable data to improve the quality of care that we provide.[6] Discrepancies in practice patterns could affect outcomes by delaying care, introducing unclear or inconsistent application of therapies, and systematic errors. The act of a clinician veering off protocol is fraught with challenges.

The study by Kallet et al[2] provides us a view into the application of adjuvant and rescue strategies. In their series, similar to other epidemiologic studies,[7,8] the most common strategies used were neuromuscular blockers, inhaled vasodilators, and prone position. As seen with other cohorts, the limited utilization of ancillary and/or adjunctive treatments in those with severe ARDS (documented on day 1) perhaps highlight the risk-averse nature and reliance on comfort (easy-to-introduce therapies) over evidence, despite repeated evidence of definite mortality benefit (ie, prone position) or potential benefit (neuromuscular blockers).[9] Perhaps physicians favor neuromuscular blockers due to the resource-intensive nature and challenges of prone position implementation. Guidance exists in the evidence that surrounds, and application of, these strategies,[10-12] yet the translation at the bedside remains challenging. It is possible that some of these interventions (eg, prone position) were implemented later during the study and thus were not reported. However, developing protocols that include rescue and/or adjuvant interventions leads to timely application and improved outcomes.[13] As we learn more about ARDS, implementation will grow ever more complex. The tailoring of therapy to phenotypes, to specific etiologies, and to different stages of the disease will only increase the challenges of implementation. One can only ponder, given the deluge of information and variables, if a clinician-driven protocol has any chance to succeed, or if, computer-based protocols (and artificial intelligence algorithms) are the safest and most efficient way to recognize[13,14] and implement care.[15,16]

Finally, we must review and analyze the data with a healthy degree of skepticism that arises out of the limitations of this retrospective observational study and its innate inability to adjust for confounders and biases. Yet, Kallet et al[2] should be lauded for their attempt to provide insight into the population with ARDS not enrolled in trials and into the practices that affect their outcomes. This study highlights that subjects with ARDS who were not enrolled in clinical trials (that is, most of our patients) were sicker and that adherence to evidence-based medicine will impact their outcomes. We argue and recommend that, in this frail and vulnerable population, the first day is essential. Our process should focus on early identification of the disease and protocolization of care for better and early dispensation of therapies with proven mortality benefit. Above all, investment into implementation strategies that facilitate early recognition and consistent institution of treatments and/or protocols are sure to yield rich clinical dividends.

Eduardo Mireles-Cabodevila
Abhijit Duggal
Sudhir Krishnan
Respiratory Institute
Cleveland Clinic
Cleveland, Ohio

REFERENCES

1. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. JAMA 2016;315(8):788-800.
2. Kallet RH, Lipnick M, Pirracchio R. ARDS outcomes in non-research subjects assessed by generalized prospective trial eligibility criteria and adherence to lung-protective ventilation. Respir Care 2021;66(9) 1380-1388.
3. Acute Respiratory Distress Syndrome Network; Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT, Wheeler A. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301-1308.
4. Pais FM, Sinha P, Liu KD, Matthay MA. Influence of clinical factors and exclusion criteria on mortality in ARDS observational studies and randomized controlled trials. Respir Care 2018;63(8):1060-1069.
5. Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. Crit Care Med 1981;9(8):591-597.
6. Morris AH. Treatment algorithms and protocolized care. Curr Opin Crit Care 2003;9(3):236-240.
7. Qadir N, Bartz RR, Cooter ML, Hough ML, Lanspa MJ, Goodspeed VM, et al. Variation in early management practices in moderate-to-severe ARDS in the United States: the severe ARDS - generating evidence study. Chest 2021;S0012-3692(21)01078-3.
8. Duggal A, Rezoagli E, Pham T, McNicholas AB, Fan E, Bellani G, et al. Patterns of use of adjunctive therapies in patients with early moderate to severe ARDS: insights from the LUNG SAFE study. Chest 2020;157(6):1497-1505.
9. Tarazan N, Alshehri M, Sharif S, Al Duhailib Z, Møller MH, Belley-Cote E, et al. Neuromuscular blocking agents in acute respiratory distress syndrome: updated systematic review and meta-analysis of randomized trials. Intensive Care Med Exp 2020;8(1):61.
10. Papazian L, Aubron C, Brochard L, Chiche J-D, Combes A, Dreyfuss D, et al. Formal guidelines: management of acute respiratory distress syndrome. Ann Intensive Care 2019;9:69.
11. Fan E, Del Sorbo L, Goligher EC, Hodgson CL, Munshi L, Walkey AJ, et al. An official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: mechanical ventilation in adult patients with acute respiratory distress syndrome. Am J Respir Crit Care Med 2017;195 (9):1253-1263.

12. Alessandri F, Pugliese F, Ranieri VM. The role of rescue therapies in the treatment of severe ARDS. Respir Care 2018;63(1):92-101.
13. Gallo de Moraes A, Holets SR, Tescher AN, Elmer J, Arteaga GM, Schears G, et al. The clinical effect of an early, protocolized approach to mechanical ventilation for severe and refractory hypoxemia. Respir Care 2020;65(4):413-419.
14. Sjoding MW, Taylor D, Motyka J, Lee E, Co I, Claar D, et al. Deep learning to detect acute respiratory distress syndrome on chest radiographs: a retrospective study with external validation. Lancet Digit Health 2021;3(6):e340-e348.
15. Wendel Garcia PD, Hofmaenner DA, Brugger SD, Acevedo CT, Bartussek J, Camen G, et al. Closed-loop versus conventional mechanical ventilation in COVID-19 ARDS. J Intensive Care Med 2021;8850666211024139.
16. Morris AH. Rational use of computerized protocols in the intensive care unit. Crit Care 2001;5(5):249-254.