REFERENCES

1. Dassner AM, Nicolau DP, Girotto JE: Management of pneumonia in the pediatric critical care unit: An area for antimicrobial stewardship. *Curr Pediatr Rev* 2017; 13:49–66
2. Elward AM, Warren DK, Fraser VJ: Ventilator-associated pneumonia in pediatric intensive care unit patients: Risk factors and outcomes. *Pediatrics* 2002; 109:758–764
3. Fayon MJ, Tucci M, Lacroix J, et al: Nosocomial pneumonia and tracheitis in a pediatric intensive care unit: A prospective study. *Am J Respir Crit Care Med* 1997; 155:162–169
4. Karsies T, Tarquinio K, Shein SL, et al; the Pediatric Acute Lung Injury and Sepsis Investigator's (PALISI) Network: Compliance With an Antibiotic Guideline for Suspected Ventilator-Associated Infection: The VAIN2 Study. *Pediatr Crit Care Med* 2021; 22:859–869
5. Levy ER, Swami S, Dubois SG, et al: Rates and appropriateness of antimicrobial prescribing at an academic children's hospital, 2007-2010. *Infect Control Hosp Epidemiol* 2012; 33:346–353
6. Kalil AC, Metersky ML, Klompas M, et al: Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016; 63:e61–e111
7. Tsou PY, Rafael J, Ma YK, et al: Diagnostic accuracy of procalcitonin for bacterial pneumonia in children - a systematic review and meta-analysis. *Infect Dis (Lond)* 2020; 52:683–697
8. Fagon JY, Chastre J, Wolff M, et al: Invasive and noninvasive strategies for management of suspected ventilator-associated pneumonia. A randomized trial. *Ann Intern Med* 2000; 132:621–630
9. Murphy CN, Fowler R, Balada-Llasat JM, et al: Multicenter evaluation of the biofire filmarray pneumonia/pneumonia plus panel for detection and quantification of agents of lower respiratory tract infection. *J Clin Microbiol* 2020; 58:e00128–e00120
10. Gastli N, Loubinoux J, Daragon M, et al; French FA-PP study group: Multicentric evaluation of BioFire FilmArray Pneumonia Panel for rapid bacteriological documentation of pneumonia. *Clin Microbiol Infect* 2020; S1198-743X(20)30710-2
11. Dellit TH, Owens RC, McGowan JE Jr, et al; Infectious Diseases Society of America; Society for Healthcare Epidemiology of America: Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007; 44:159–177
12. Di Pentima MC, Chan S: Impact of antimicrobial stewardship program on vancomycin use in a pediatric teaching hospital. *Pediatr Infect Dis J* 2010; 29:707–711
13. Di Pentima MC, Chan S, Hossain J: Benefits of a pediatric antimicrobial stewardship program at a children's hospital. *Pediatrics* 2011; 128:1062–1070
14. Newland JG, Stach LM, De Lurgio SA, et al: Impact of a prospective-audit-with-feedback antimicrobial stewardship program at a children's hospital. *J Pediatric Infect Dis Soc* 2012; 1:179–186

Driving Pressure and Mechanical Power: The Return of Physiology in Pediatric Mechanical Ventilation*

KEY WORDS: acute respiratory distress syndrome; children; driving pressure; mechanical power; mechanical ventilation

Martin C. J. Kneyber, MD, PhD, FCCM[1,2]

Our understanding how to use mechanical ventilation (MV) has much improved over the recent decades. Considerable focus is being placed on evolving concepts including driving pressure (DP) and mechanical power (MP), which can provide a more individualized approach to ventilatory management (1). These concepts have also gained interest in the pediatric critical care community, which immediately raises the question of whether the data from adults apply to critically ill children. In this issue of *Pediatric Critical Care Medicine*, Diaz et al (2) studied DP and MP in a post hoc analysis of data collected in 30 children undergoing general anesthesia and 38 with Pediatric Acute Lung Injury Consensus Conference defined pediatric acute respiratory distress syndrome (PARDS). DP and MP were significantly higher in PARDS patients,

***See also p. 870.**

DOI: 10.1097/PCC.0000000000002829

but the real message is that it makes us ask ourselves how we should interpret DP and MP in PARDS?

Early knowledge on ventilator management came from the operating theater, where the goal was to achieve normal gas exchange and prevent atelectasis. Then, in the early days of critical care medicine, the common approach was to deliver large tidal volumes (VT), ranging from 10 to 15 mL/kg, "without causing pulmonary damage," but such was the risk of barotrauma that "prophylactic tube thoracostomies" were considered (3–5). Building on earlier practices and observations, linking supraphysiologic VT to the development of ventilator-induced lung injury (VILI), the Acute Respiratory Distress Syndrome (ARDS) Network conducted their landmark trial comparing 6 mL/kg predicted bodyweight (PBW) combined with limiting plateau pressures (Pplat) to 30 cm H_2O versus 12 mL/kg PBW and Pplat to 50 cm H_2O (6, 7). Mortality in the low VT was 9% less, giving rise to the concept of lung-protective ventilation (LPV). LPV entails using low VT, but it remains unclear what "low" really means since in adult ARDS comparing 6 versus 10 mL/kg PBW or 7 versus 10 mL/kg PBW have not shown mortality benefit (8). We also have to remember the impact of the problem of lung heterogeneity in ARDS pathology. Here, we think of the degree of normally aerated tissue being much smaller (i.e., the "baby lung") (9). Such heterogeneity may lead to regional tidal overdistension, even if 6 mL/kg PBW VT is used, indicating that much smaller VT is necessary in some patients (10).

Based on the baby lung concept (i.e., respiratory system compliance [CRS] is linearly related to the amount of inflatable lung volume), Amato et al (11) hypothesized that scaling VT to CRS would better correlate with lung stress and patient outcome. Through multilevel mediation analyses of data from 3,562 patients with ARDS enrolled in nine randomized controlled trials (RCTs), the authors showed that higher DP was associated with increased mortality and that reducing DP by limiting Pplat and increasing positive end-expiratory pressure (PEEP) was associated with increased survival. Taking this concept one step further, Gattinoni et al (12) introduced MP as a measure and potential driver of VILI. The formula to calculate MP was based on the equation of motion and reflects the energy per breathing cycle multiplied by ventilation frequency delivered to the respiratory system (13).

The concept of DP and MP are illustrative of the contemporary, physiology-driven way of thinking about MV, although it is unclear if these parameters drive VILI or simply reflect disease severity (1). There are no RCTs that demonstrate DP or MP improved outcome when a ventilator strategy focused on DP or MP in adult ARDS. Limiting DP and MP requires reducing VT and/or increasing PEEP. However, unlike management of supportive ventilation in adults, we have yet to prove that large VT ventilation leads to VILI in children (14). We do know from observational data that there is a direct relationship between VT and better outcome, and experimental models suggest an age-related susceptibility to VILI; in other words, the larger the VT, the better the outcome (14–16). For PEEP, we know that pediatric critical care practitioners tend to use low levels of PEEP and inherently accept higher FIO_2, although such practices may lead to worse outcomes (17–19).

Not a single threshold of VT has been associated with mortality in mechanically ventilated children with or without ARDS (20). These above observations may be explained by the preferential use of a pressure controlled (PC) mode of ventilation in children. Importantly, DP and MP were developed in adult ARDS patients ventilated with a volume controlled (VC) mode of ventilation. By design, this mode has a constant inspiratory flow and a zero flow state generating Pplat. PC ventilation does not have a zero flow state and does not generate Pplat. Peak inspiratory pressure is dependent on the resistive properties of the respiratory system and therefore a poor surrogate of Pplat (21). For VC, the operator sets the VT, but for PC, the operator sets the inspiratory pressure and the delivered VT is dictated by CRS (22). Thus, the lower the compliance, the lower the VT will be for a given pressure. It may therefore be surmised that in pediatrics, the concept of DP unknowingly already has been applied to a certain degree. Provocatively, this would strongly suggest abandoning any ventilator mode to requires the operator to set a certain VT in patients with lung injury. Diaz et al (2) found higher DP among PARDS patients, but the clinical meaning of these observations was not addressed.

In their contribution, Diaz et al (2) also addressed the problem that two key components of MP (i.e., VT and respiratory rate [RR]) are age dependent (i.e., the older the child, the larger the VT and the lower the RR), making injurious thresholds for MP not uniform across the pediatric age-range and poorly reflecting underlying lung pathology (2, 23). This calls for normalization of

MP, since they nicely showed that without normalization MP was comparable between patients with and without PARDS. Nonetheless, it remains to be determined if normalization to Crs might be a better alternative as has been observed in adult ARDS (24).

DP and MP teach us that ventilation is about physiology and that one approach does not suit all cases of PARDS. While we do not have data on injurious thresholds for these indices, being aware of the many limitations of them, and the fact that we do not know what the best Vt and PEEP is, it seems appropriate to incorporate these ideas into our daily practice. Ventilate gently, limit stress and strain and do not generate too much heat.

1 *Department of Paediatrics, Division of Paediatric Critical Care Medicine, Beatrix Children's Hospital, University Medical Center Groningen, The University of Groningen, Groningen, The Netherlands*

2 *Critical Care, Anaesthesiology, Peri-Operative & Emergency Medicine, The University of Groningen, Groningen, The Netherlands*

Dr. Kneyber has disclosed that he does not have any potential conflicts of interest.

REFERENCES

1. Menk M, Estenssoro E, Sahetya SK, et al: Current and evolving standards of care for patients with ARDS. *Intensive Care Med* 2020; 46:2157–2167
2. Diaz, F, González-Dambrauskas S, Cristiani F, et al: Driving Pressure and Normalized Energy Transmission Calculations in Mechanically Ventilated Children Without Lung Disease and Pediatric Acute Respiratory Distress Syndrome. *Pediatr Crit Care Med* 2021; 22:870–878
3. Bendixen HH, Hedley-Whyte J, Laver MB: Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. A concept of atelectasis. *N Engl J Med* 1963; 269:991–996
4. Pontoppidan H, Geffin B, Lowenstein E: Acute respiratory failure in the adult. 3. *N Engl J Med* 1972; 287:799–806
5. Steier M, Ching N, Roberts EB, et al: Pneumothorax complicating continuous ventilatory support. *J Thorac Cardiovasc Surg* 1974; 67:17–23
6. Brower RG, Matthay MA, Morris A, et al; Acute Respiratory Distress Syndrome Network: 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; 342:1301–1308
7. Dreyfuss D, Saumon G: Ventilator-induced lung injury: Lessons from experimental studies. *Am J Respir Crit Care Med* 1998; 157:294–323
8. Eichacker PQ, Gerstenberger EP, Banks SM, et al: Meta-analysis of acute lung injury and acute respiratory distress syndrome trials testing low tidal volumes. *Am J Respir Crit Care Med* 2002; 166:1510–1514
9. Gattinoni L, Pesenti A: The concept of "baby lung." *Intensive Care Med* 2005; 31:776–784
10. Terragni PP, Rosboch G, Tealdi A, et al: Tidal hyperinflation during low tidal volume ventilation in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2007; 175:160–166
11. Amato MB, Meade MO, Slutsky AS, et al: Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med* 2015; 372:747–755
12. Gattinoni L, Marini JJ, Collino F, et al: The future of mechanical ventilation: Lessons from the present and the past. *Crit Care* 2017; 21:183
13. Marini JJ, Rocco PRM, Gattinoni L: Static and dynamic contributors to ventilator-induced lung injury in clinical practice. Pressure, energy, and power. *Am J Respir Crit Care Med* 2020; 201:767–774
14. Kneyber MC, Zhang H, Slutsky AS: Ventilator-induced lung injury. Similarity and differences between children and adults. *Am J Respir Crit Care Med* 2014; 190:258–265
15. Khemani RG, Conti D, Alonzo TA, et al: Effect of tidal volume in children with acute hypoxemic respiratory failure. *Intensive Care Med* 2009; 35:1428–1437
16. Erickson S, Schibler A, Numa A, et al; Paediatric Study Group; Australian and New Zealand Intensive Care Society: Acute lung injury in pediatric intensive care in Australia and New Zealand: A prospective, multicenter, observational study. *Pediatr Crit Care Med* 2007; 8:317–323
17. Khemani RG, Markovitz BP, Curley MAQ: Characteristics of children intubated and mechanically ventilated in 16 PICUs. *Chest* 2009; 136:765–771
18. Santschi M, Jouvet P, Leclerc F, et al; PALIVE Investigators; Pediatric Acute Lung Injury and Sepsis Investigators Network (PALISI); European Society of Pediatric and Neonatal Intensive Care (ESPNIC): Acute lung injury in children: Therapeutic practice and feasibility of international clinical trials. *Pediatr Crit Care Med* 2010; 11:681–689
19. Khemani, RG, Parvathaneni, K, Yehya, N, et al: Positive end-expiratory pressure lower than the ARDS network protocol is associated with higher pediatric acute respiratory distress syndrome mortality. *Am J Respir Crit Care Med* 2018; 198:77–89
20. de Jager P, Burgerhof JG, van Heerde M, et al: Tidal volume and mortality in mechanically ventilated children: A systematic review and meta-analysis of observational studies*. *Crit Care Med* 2014; 42:2461–2472
21. Ilia S, van Schelven PD, Koopman AA, et al: Effect of endotracheal tube size, respiratory system mechanics, and ventilator settings on driving pressure. *Pediatr Crit Care Med* 2020; 21:e47–e51
22. Sahetya SK, Mancebo J, Brower RG: Fifty years of research in ARDS. Vt selection in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2017; 196:1519–1525
23. Kneyber MCJ, Ilia S, Koopman AA, et al: Energy transmission in mechanically ventilated children: A translational study. *Crit Care* 2020; 24:601
24. Coppola S, Caccioppola A, Froio S, et al: Effect of mechanical power on intensive care mortality in ARDS patients. *Crit Care* 2020; 24:246