Pediatric acute respiratory distress syndrome and new pediatric outcomes

Source: Keim, G; Watson, RS; Thomas NJ; Yehya, N. New Morbidity and Discharge Disposition of Pediatric Acute Respiratory Distress Syndrome Survivors. Crit Care Med 2018; 46:1731–1738.

ediatric acute respiratory distress syndrome (PARDS) causes significant disease burden in Pediatric Intensive Care Units (PICUs) with a reported prevalence of close to 3%¹ and short-term mortality rates up to 20%². However, following PICUs tendency to exchange higher mortality rates for higher morbidity rates, PARDS research needs to focus on data about survivors and mortality cannot be the only outcome.

The article uses a scale created as an outcome measure for use in pediatric research called the Functional Status Scale (FSS). New morbidity is defined as a 3 point increase in the scale. The authors aimed to determine new morbidity rate using change in FSS, hospital discharge disposition and 1 and 3 year mortality for survivors of PARDS. Also, researchers tried to establish epidemiologic, physiologic and treatment factors associated with these outcomes.

The cohort consisted of consecutive PICU patients from the Children's Hospital of Philadelphia's (CHOP), eligible between July 1, 2011 and December 31, 2014, who met the former criteria for Acute Lung Injury. There is a new definition for PARDS since 2015, but all patients would even though meet this diagnosis. The following data were collected in the study: demographics data, Pediatric Risk of Mortality (PRISM) III, preillness FSS and at hospital discharge, ventilator settings and Pao2/Fio2 at PARDS onset and 24 hours, laboratory data, medications for the first 3 days of PARDS and nonpulmonary organ failures at time of PARDS diagnosis. The main outcome was status at hospital discharge, trichotomized to alive without new morbidity, alive with new morbidity, and dead.

Among the 316 patients diagnosed with PARDS, the inhospital mortality rate was 13,3%. Survivors accounted for 274 patients – 77% survived without new morbidity and 23% survived with new morbidity. Those outcomes correlated well with severity of illness, non-pulmonary organ failures and severity of PARDS at 24 hours. There was a stepwise increase in each of these severity of illness markers, with survivors without new morbidity demonstrating better values, non- survivors the worst, and survivors with new morbidity having intermediate values. They divide the outcomes as good (alive without new morbidity) versus poor (new morbidity or death), and poor outcome was associated with PRISM III, nonpulmonary organ failures, immunocompromising comorbidities, and oxygenation and ventilator pressures 24 hours after PARDS onset.

Within the survivors, 72,3% were discharged home, 24,5% needed rehabilitation and 3,3% where transferred to chronic care facilities. A FSS greater than

or equal to 3 was strongly associated with discharge to rehabilitation, with highest declines in feeding, motor and respiratory functional domains. Regarding respiratory outcomes, 20,4% (56 patients) of hospital survivors had change in FSS. Of these, 19 patients underwent tracheostomy placement. Of the 56 patients with a change in respiratory FSS, 17 (30.4%) had improvement in their respiratory FSS by 3-year follow-up, 10 (17.9%) had returned to a nonmorbid FSS of 1, but seven died within the first year after PARDS and one additional patient died by 3-year follow-up. One and three-year mortality were 5,5% and 8%, respectively. One- and 3-year mortality in survivors of PARDS was most strongly predicted by immunocompromised status and higher baseline FSS, with weaker association with PRISM III score, suggesting baseline disease would influence more than PARDS itself to the prognosis.

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The issue discussed in this article is extremely important, since PARDS continues to be an important syndrome in PICU, affecting 3%¹ of PICUs patients. With increasing technology, advances in the use of extracorporeal membrane oxygenation (ECMO), protective ventilatory strategies and understanding of PARDS pathophysiology, mortality has lowered and survival with new morbidities is becoming a more robust outcome to be measured. The FSS is a functional status outcome measure for large studies that is well defined, quantitative, rapid, reliable, objective and suitable for a wide spectrum of ages. It includes 6 domains: mental status, sensory, communication, motor, feeding and respiratory, categorized from normal (I) to very severe dysfunction (5)³.

It is the first study relating PARDS and functional outcomes. The authors showed that variables associated with inhospital mortality also related to new morbidity and new morbidity exists on an intermediate step along the continuum of intact survival to death. FSS seems to be a useful outcome measure in PARDS. These results confirm previous findings from a large study from Pollack et al⁴, which showed that increasing PRISM III scores was also associated with development of new morbidity and that new morbidity was a more common outcome than mortality⁵.

A cornerstone of improving critical care is early mobilization and rehabilitation^{6,7}. CHOP had a well-developed rehabilitation center and the integration of early physical therapy services and an active rehabilitative medicine team with an associated inpatient rehabilitation unit may have contributed to better outcomes without new morbidity and early return to basal FSS after hospital discharge. Follow-up FSS scores would be helpful in knowing the effect of the rehabilitation interventions on the dysfunction associated with PARDS.

Finally, detecting new morbidities allows for the study of new interventions to reduce the consequences of PICU hospitalization, not only related to the disease itself, but also to the intensive care provided, making studies like these increasingly important.

References

- I. Khemani RG, Smith L, Lopez-Fernandez YM, Kwok J, Morzov R, Klein MJ, Yehya N, Willson D, Kneyber MCJ, Lillie J, Fernandez A, Newth CJL, Jouvet P, Thomas NJ; Pediatric Acute Respiratory Distress syndrome Incidence and Epidemiology (PARDIE) Investigators; Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network.; Pediatric acute respiratory distress syndrome incidence and epidemiology (PARDIE): an international, observational study. Lancet Respir Med. 2018 Oct 22. pii: S2213-2600(18)30344-8.
- **2.** Yehya N, Bhalla AK, Thomas NJ, et al: Alveolar dead space fraction discriminates mortality in pediatric acute respiratory distress syndrome. Pediatr Crit Care Med 2016; 17:101–109.
- 3. Pollack MM, Holubkov R, Glass P., Dean JM, Meert KL, Zimmerman J, Anand KJS, Carcillo J, Newth CJL, Harrison R, Willson DF, Nicholson C and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Collaborative Pediatric Critical Care Research Network (CPCCRN); The Functional Status Score (FSS): A New Pediatric Outcome Measure. Pediatrics. 2009 July; 124(I): e18–e28.
- **4.** Pollack MM, Holubkov R, Funai T, et al. Simultaneous prediction of new morbidity, mortality, and survival without new morbidity from pediatric intensive care: a new paradigm for outcomes assessment. Crit Care Med 2015;43(8):1699–709.
- **5.** Pollack MM, Holubkov R, Funai T et al. for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. Pediatric Intensive Care Outcomes: Development of New Morbidities During Pediatric Critical Care. Pediatr Crit Care Med 2014; 15:821–827.
- **6.** Wieczorek B., Burke C., Al-Harbi A., Kudchadkar SR. Early mobilization in the pediatric intensive care unit: a systematic review; J Pediatr Intensive Care. 2015; 2015: 129–170. doi:10.1055/s-0035-1563386.
- **7.** Hopkins RO, Choong K, Zebuhr CA, Kudchadkar SR. Transforming PICU Culture to Facilitate Early Rehabilitation. J Pediatr Intensive Care. 2015;4(4):204-211.