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Commentary

Optimizing surveillance for pediatric ventilator-associated events—But are they preventable?

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Ventilator-associated infections (VAIs), such as ventilator-associated pneumonia (VAP) or tracheobronchitis (VAT), are common complications among patients requiring artificial airways and invasive mechanical ventilation. However, these infections have overlapping symptomatology with other respiratory pathologies and remain difficult to define using easily obtained and objective clinical parameters.[1] In an effort to identify preventable harm in a way that is feasible and meaningful to monitor across health systems, the US Centers for Disease Control (CDC) surveillance definitions have shifted from VAP to ventilator-associated events (VAEs) with objective criteria for specific ventilator-support cutoffs and secondary consideration of infectious etiology constituting possible VAP. In 2013, the CDC shifted the adult VAP definition to this new VAE approach and an adapted pediatric VAE definition was formally put into place in January 2019.[2] Another definition for pediatric VAE using less stringent parameters was proposed in 2019 by Peña-López et al.[3]

In a study published in this issue of *Infection Control and Hospital Epidemiology*, Papakyritsi et al[2] applied 3 VAE definitions: the CDC adult VAE definition, the CDC pediatric VAE definition, and the VAE definition proposed by Peña-López, referred to as the "European pediatric VAE" definition.[3] The study was conducted with a retrospective cohort of mechanically ventilated children in a pediatric intensive care unit (PICU) in Greece to characterize the incidence of VAE, as identified by the 3 definitions and their association with mortality.[4] The study had 2 primary findings. First, both CDC definitions detected lower incidences of VAE than the European definition when applied to this cohort of PICU patients. Specifically, among 290 mechanically ventilated children, rates of VAE were 4.7 per 1,000 ventilator days using the CDC adult VAE definition, 6 per 1,000 ventilator days using the CDC pediatric VAE definition, and 9.7 per 1,000 ventilator days using the European pediatric VAE definition. Second, all 3 definitions of VAE had similar associations with clinical outcomes. In a multivariate regression model, patients in whom VAE was identified using any of the three definitions had significantly increased odds of mortality (odds ratios of 8.7, 6.9, and 4.0, respectively) compared to patients without VAE. In a univariate analysis across the 3 VAE definitions, patients with VAE had similarly longer mechanical ventilation (27.5, 27.5, 26 days, respectively) and increased PICU length of stay (28.5, 28, 27 days, respectively).

This study is the first to directly compare the incidence rates and clinical outcomes of mortality across these 3 definitions, particularly comparing the CDC pediatric VAE and European pediatric VAE criteria. A limitation of the study is that it applied these definitions retrospectively to a cohort of PICU patients in a single center in Greece who had relatively high acuity. Thus, whether the same associations with mortality, length of stay and duration of ventilation would be reproduced in different PICU populations is unknown.

Despite the single-center design, comparison of these VAE definitions contributes to the debate regarding an optimal surveillance approach for VAE in PICU patients. This study highlights how incidence rates are highly dependent on the parameters used to define VAE. The lower cutoffs for PEEP, FiO_2, and duration of decline (using 1 day of decline instead of 2 days) included in the European VAE criteria resulted in a higher incidence of VAE when this definition was applied. One concern regarding the CDC pediatric VAE definition is that it may not be sensitive to clinically diagnosed VAI[5] and instead may be capturing only the most severe cases of pulmonary pathology with significantly impaired oxygenation or ventilation. Therefore, application of the CDC pediatric VAE definition may miss detection of more mild but clinically impactful events.[6] Papakyritis et al suggested that because the European pediatric VAE definition uses lower cutoff values for FiO_2 and PEEP than the CDC adult VAE FiO2/PEEP and CDC pediatric VAE FiO_2 values, it may be more sensitive and thus may detect more mild cases, which may facilitate identification of a higher proportion of potentially preventable events.

The investigators in the original study defining the CDC pediatric VAE criteria recommended the FiO_2 and mean airway pressure (MAP) cutoffs after considering the rates of VAE and association with worse clinical outcomes across pediatric ICU types, including cardiac and neonatal ICUs.[7] However, they acknowledged an "expectation that further information about etiology, risk factors, and degree of preventability would lead to future refinements." Another consideration is that in the pediatric and neonatal population, high frequency ventilation (HFV) via oscillatory or jet ventilation is more common than in adult populations, and using measures of PEEP, as in the European pediatric VAE criteria, instead of using MAP, as in the CDC pediatric VAE criteria, would inherently exclude patients receiving, or transitioning to, high frequency ventilation. (Such patients are currently

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excluded by the CDC adult VAE definition.) Indeed, 3 of the children meeting the CDC pediatric VAE criteria did not meet the other 2 criteria, likely related to inclusion of MAP in the CDC pediatric VAE criteria. Also, since MAP is a measured variable and PEEP is set, there is inherently more variation in MAP over time, leading to more variability in minimum daily values and lower likelihood of establishing a baseline, thereby potentially lowering the sensitivity of MAP-based definitions.

Lower cutoff values for ventilator support settings will certainly identify more instances of VAE. What has been demonstrated across all the VAE definitions is that, unlike the original VAP definitions, the VAE criteria that focus on oxygenation and respiratory mechanics are consistently associated with worse clinical outcomes.[3,4,7] Unfortunately, clinical consensus regarding what constitutes a true ventilator-associated infection deserving antibiotic treatment is still lacking. Furthermore, because VAP can have minimal impact on respiratory physiology and gas exchange, it is perhaps not surprising that many VAP cases are missed by all of the current VAE definitions. VAE surveillance also identifies noninfectious conditions, such as fluid overload, pulmonary hypertension, pulmonary hemorrhage, and inflammatory reactions like ARDS, which are all important etiologies of respiratory dysfunction in critically ill patients. Indeed, most pediatric VAE are not related to infection; thus, additional risk factors for pediatric VAEs exist beyond those associated with VAP.[8] Positive fluid balance, acute kidney injury, neuromuscular blockade, sedative type, and blood transfusions have variably been associated with pediatric VAEd in studies using either the CDC or European pediatric VAE criteria.[9–12] Thus, VAE likely better reflects lung dysfunction compared to prior VAP definitions, but it is not specific to the underlying etiology. As the goal of surveillance has moved away from focusing purely on infectious etiologies and toward identifying all potentially preventable harms, the optimal surveillance definition would identify true cases of pathology and generate metrics that can be used to guide prevention efforts.

With the iterations of VAE definitions, another question has been proposed: would a more sensitive definition have a better association with preventability and modifiable risk factors? Analogous questions have arisen between metrics such as central-line–associated infections (CLABSIs) and hospital-onset bacteremia (HOB). For example, CLABSIs exclude bacteremia events that are not associated with a central line, but these HOB infections lead to significant patient harm and may also be preventable. More recently, HOB has been suggested as an outcome measure having potentially greater ability to discriminate hospital performance than CLABSI,[13] and the preventability of HOB as an outcome is sensitive to modifications in healthcare processes.[14] Drawing some parallel with consideration of bloodstream infections, optimal surveillance methods for VAE will employ definitions that (1) can capture the majority of relevant cases associated with patient harm, (2) can be implemented across diverse hospital systems, and importantly, (3) identify outcomes that are amenable to improvement with prevention strategies. Of these surveillance measure characteristics, the last point remains underdeveloped in the case of pediatric VAE.

Studies have assessed whether measures such as spontaneous breathing trials can prevent VAEs among adults.[15] However, no similar published studies have been conducted among pediatric populations. Prospective, multicenter studies evaluating the impact of defined interventions may further indicate whether a more or less sensitive definition of VAE would be useful for comparing hospital performance and for monitoring response to implemented changes in patient care. The Solutions for Patient Safety Network has used the CDC pediatric VAE definition to test potential VAE prevention bundle elements, including daily discussion of extubation readiness (to shorten the duration of mechanical ventilation) and daily discussion of fluid balance goals (to avoid fluid overload), among a cohort of 16 hospitals with results expected in 2022.[16] Future studies should assess both pediatric VAE definitions to determine whether more sensitive definitions are associated with greater improvement in clinical processes to prevent patient harm.

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