OPEN

Association Between Critical Events in the PICU and Outcomes in Neighboring Patients

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OBJECTIVE: PICU patients who experience critical illness events, such as intubation, are at high risk for morbidity and mortality. Little is known about the impact of these events, which require significant resources, on outcomes in other patients. Therefore, we aimed to assess the association between critical events in PICU patients and the risk of similar events in neighboring patients over the next 6 hours.

DESIGN: Retrospective observational cohort study.

SETTING: Quaternary care PICU at the University of Chicago.

PATIENTS: All children admitted to the PICU between 2012 and 2019.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: The primary outcome was a critical event defined as the initiation of invasive ventilation, initiating vasoactive medications, cardiac arrest, or death. The exposure was the occurrence of a critical event among other patients in the PICU within the preceding 6 hours. Discrete-time survival analysis using fixed 6-hour blocks beginning at the time of PICU admission was used to model the risk of experiencing a critical event in the PICU when an event occurred in the prior 6 hours. There were 13,628 admissions, of which 1,886 (14%) had a critical event. The initiation of mechanical ventilation was the most frequent event ($n = 1585$; 59%). In the fully adjusted analysis, there was a decreased risk of critical events (odds ratio, 0.82; 95% CI, 0.70–0.96) in the 6 hours following exposure to a critical event. This association was not present when considering longer intervals and was more pronounced in patients younger than 6 years old when compared with patients 7 years and older.

CONCLUSION: Critical events in PICU patients are associated with decreased risk of similar events in neighboring patients. Further studies targeted toward exploring the mechanism behind this effect as well as identification of other nonpatient factors that adversely affect outcomes in children are warranted.

KEY WORDS: electronic health records; intensive care unit; quality improvement; risk assessment

PICU patients who suffer critical events, such as being ventilated or experiencing cardiac arrest, have a significantly higher risk of mortality and worse long-term outcomes.(1-5) Along with patient-level risk factors, studies have also identified unit-level risk factors that are associated with poor outcomes among PICU patients.(6, 7) Within adults, it has been shown that the occurrence of a cardiac arrest, death, or a direct ward to ICU transfer increases the likelihood of similar events in other patients on the same ward, within the next 6 hours.(8) These events tend to disrupt normal hospital workflow and could result in inadequate care for neighboring patients thereby increasing their risk of poor outcomes. Extrapolating these results from adult inpatients to

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children admitted to the PICU is not straightforward. For instance, providers in the PICU may be better equipped to deal with the occurrence of critical events. Additionally, rates of outcomes, disease characteristics, and treatment strategies in children do not follow the same patterns as adult patients.(4, 9-11) At present, no study has assessed the association between the occurrence of a critical event in the PICU and outcomes in other PICU patients.

The aim of this study was to determine the association between critical events in PICU patients and the risk of similar events in neighboring patients over the next 6 hours. We define critical events in the PICU as the occurrence of cardiac arrest, initiation of mechanical ventilation, initiation of vasoactive drugs, or death. We hypothesize that critical events in PICU patients are associated with increased risk of critical events in neighboring patients over the next 6 hours. Determining the nature of this association could lead to a better understanding of the influence of critical events in the PICU and create opportunities to mitigate any harmful effects.

MATERIALS AND METHODS

Setting and Study Population

We conducted an observational cohort study of all pediatric admissions (age < 18 yr) to the PICU at University of Chicago Comer Children's Hospital from January 1, 2012, to December 31, 2019. Comer Children's Hospital is a tertiary care center with approximately 1,500 ICU admissions every year. Patients who were admitted to the PICU for less than 4 consecutive hours were excluded from the study sample as these were indicative of transitory patients or errors in documented location, for example, single recordings of vital signs. The study was initially approved by the University of Chicago Institutional Review Board (IRB no. 18-0645, Title: Novel Predictors of Clinical Deterioration in Hospitalized Children) on May 14, 2019, with a waiver of informed consent granted, and all annual continuing reviews have been approved. Study procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975.

Data Sources

Data were extracted from the Clinical Research Data Warehouse, which is maintained by the Center for Research Informatics at the University of Chicago. Clinical data for patients were collected from the electronic health record (EHR; Epic, Verona, WI), whereas patient demographics and disposition information were obtained from administrative data.

Exposure and Outcome Variables

We define a critical event as the initiation of mechanical ventilation that was greater than 24 hours, the first administration of vasoactive medications (dobutamine, dopamine, epinephrine, milrinone, norepinephrine, and vasopressin), cardiac arrest, or death. Data for death, initiation of mechanical ventilation, and vasoactive medication were extracted from the EHR. Initiation of mechanical ventilation events were identified based on flowsheet recording of mechanical ventilation that was preceded by a flowsheet recording of nonmechanical ventilation (e.g., room air, high-flow nasal cannula, etc.). Data did not differentiate between patients who were placed on mechanical ventilation after urgent intubation and those who were routinely placed on mechanical ventilation via tracheostomy tube. The requirement that mechanical ventilation events should last at least 24 hours to be considered as a critical event excludes routine night-time ventilation events which are potentially less disruptive. Cardiac arrest data were obtained from a separate database maintained as a component of routine monitoring of in-hospital cardiac events for quality improvement initiatives. The primary outcome was the occurrence of at least one critical event in a PICU patient in the following 6 hours. The primary exposure was whether there was at least one critical event in another patient in the PICU in the prior 6 hours. Based on frequency analysis of events, the outcome and exposure were coded as binary variables, with 0 indicating no events and 1 indicating at least one critical event. Because our exposure and outcomes are binary, multiple instances of events for a single patient over a 6-hour interval were considered as an exposure (or outcome) of 1, indicative of at least one event. Further, the occurrence of an event for a patient was not counted as exposure for the same patient.

Statistical Analysis

We used logistic regression within a discrete time survival analysis framework to determine the association between critical events and the outcomes of other patients in the PICU within the next 6 hours. Briefly, we divided data longitudinally into sequential, nonoverlapping, 6-hour intervals and measured the association between occurrences of critical events within an interval and outcomes within the next 6-hour interval. We adjusted for patient severity of illness through the Pediatric Risk of Mortality (PRISM score), time of day (day: 7 AM to 7 PM vs night: 7 PM to 7 AM), weekday versus weekend, and the ICU census at the time of the event. Using individual 6-hour time periods as the unit of analysis, sequential logistic regression adjustments were conducted to understand how variables impact the association between critical events and outcomes in the PICU within the next 6 hours. The model was adjusted in the following order: demographics, patient's PRISM score, the time of day and the day of week, PICU census, average PRISM score of all patients in the unit, and last, year and season. We also considered 12- and 18-hour time periods apart from the 6-hour window.

A sensitivity analysis was also conducted for different age groups (i.e., 0–2, 3–6, 7–11, and > 11 yr) using the fully adjusted logistic regression model that used the 6-hour period. Additionally, for a deeper analysis of event-specific exposure and outcomes, we conducted a frequency analysis of different types of exposures and outcome within the next 6 hours. We also analyzed the distribution of outcomes during the 18-hour period following the exposure event. Finally, to assess potential long-term impact of being exposed to a critical event, we compared the mortality and length of stay of patients for different rates of exposure to critical events during a patient's hospital stay. A two-sided p value of less than 0.05 was used to denote statistical significance. All analyses were performed using R, version 3.6 (R Project for Statistical Computing, Vienna, Austria).

RESULTS

Of the 13,628 ICU admissions during the study period, 1,886 (14%) experienced critical events from 2012 to 2019 (**Table 1**). Patients who experienced critical events were younger (mean age 5 vs 6 yr; $p < 0.001$), less likely to be Black (56% vs 61%; $p < 0.001$), more likely to be of Hispanic ethnicity (14% vs 11%, $p < 0.001$), have a higher mean PRISM score (6 vs 1; $p < 0.001$), and have longer median length of stay (6 d vs 1 d, $p < 0.001$).

The most frequent critical event in our cohort was the initiation of mechanical ventilation that occurred 1,585 times (12% of all admissions). This was followed by the initiation of vasoactive support which had 832 occurrences (6% of admissions). There were 104 documented cardiac arrests (1% of admissions) and 178 deaths (1% of admissions).

In our unadjusted analysis, the likelihood of a critical event in a patient was lower (odds ratio [OR], 0.81; 95% CI, 0.69–0.94) in the 6 hours after exposure to at least one critical event among other patients in the PICU. The association persisted after adjustment for the patient's age, sex, race, and ethnicity (OR, 0.81;

TABLE 1.
Comparison of Characteristics of Patients Who Had Critical Events With Those Who Did Not

Patient Characteristic		ICU Admissions With Critical Events (1,886)	ICU Admissions Without Critical Events (11,742)	p
Female sex, *n* (%)		825 (44)	5,343 (46)	0.161
Age, yr, mean (SD)		5 (6)	6 (6)	< 0.001
Race, *n* (%)	Black	1,059 (56)	7,122 (61)	< 0.001
	White	542 (29)	3,044 (26)	
	Other	285 (15)	1,576 (13)	
Hispanic Ethnicity, *n* (%)		272 (14)	1,335 (11)	< 0.001
Pediatric Risk of Mortality score, mean (SD)		6 (5)	1 (2)	< 0.001
Length of stay, median (interquartile range)		6 (3–12)	1 (1–3)	< 0.001

95% CI, 0.69–0.94), PRISM score (OR 0.80, 95% CI: 0.69—0.93), time of the day and the day of the week (OR, 0.82; 95% CI, 0.69–0.95), ICU census (OR, 0.81; 95% CI, 0.70–0.94), average ICU severity of illness (OR, 0.82; 95% CI, 0.70–0.96), and season and year (OR, 0.81; 95% CI, 0.70–0.95) when compared with the unadjusted result (**Table 2**). **Supplementary Table 1**, (http://links.lww.com/CCX/B59) depicts the final ORs of all variables in the fully adjusted model.

Critical events were distributed uniformly across the 18 hours after a critical exposure event (**Supplementary Fig. 1**, http://links.lww.com/CCX/B59). When assessed 12 hours after the exposure event, the decreased likelihood of a subsequent critical event was noted (OR, 0.84; 95% CI, 0.75–0.95). At 18 hours after the exposure event, there was no association (OR, 0.93; 95% CI, 0.83–1.04) between prior exposure to events in the PICU and subsequent event for the patient. These findings are presented in **Figure 1**. We observed no significant association between our primary exposure and outcome when considering a 4-hour window (OR, 1.03; 95% CI, 0.86–1.22). We further performed a secondary analysis where we considered exposure types of zero events, one patient with at least one event, or more than one patient with at least one event. In this patient-level analysis, we merge multiple events for the same patient over a 6-hour window. After adjusting for confounders, we detected a decreased risk for another patient to experience an event after exposure to a PICU event (OR, 0.82; 95% CI, 0.69–0.96) and a similar but nonsignificant OR for more than one patient to experience events (OR, 0.79; 95% CI, 0.55–1.09), although this analysis is likely to be underpowered.

TABLE 2.
Odds Ratios With 95% CIs Depicting the Association Between Occurrence of Critical Events and Outcome With Sequential Adjustment for Patient- and Unit-Level Factors

Models	OR (95% CI)
Model 1: Unadjusted	0.81 (0.69–0.94)
Model 2: Model 1 + age, sex, race, ethnicity	0.81 (0.69–0.94)
Model 3: Model 2 + patient's PRISM score	0.80 (0.69–0.93)
Model 4: Model 3 + weekend and night shift	0.82 (0.69–0.95)
Model 5: Model 4 + ICU census	0.81 (0.70–0.94)
Model 6: Model 5 + average ICU PRISM score	0.82 (0.70–0.96)
Model 7: Model 6 + year and season	0.81 (0.70–0.95)

OR = odds ratio, PRISM = Pediatric Risk of Mortality.
+ indicates addition of variable to the the model from the above row.

Sensitivity analysis revealed varying associations between outcome in a patient and being exposed to a critical event based on age (**Table 3**). Occurrence of critical events in the PICU was associated with decreased risk of the primary outcome by a greater magnitude in patients between ages 3 and 6 years (OR, 0.61; 95% CI, 0.39–0.92) in comparison with children who were less than 2 years (OR, 0.80; 95% CI, 0.64–0.98) or between 7 and 11 years (OR, 0.80; 95% CI, 0.48–1.25). There was no association between being exposed to critical events and subsequently experiencing a critical event among children older than eleven years old (OR, 1.04; 95% CI, 0.74–1.43).

Patients who were exposed to at least one critical event during their ICU stay had a significantly lower ICU mortality than those who had no exposure (0.9% vs 2.1%; $p < 0.001$). There was no significant association between the mean length of ICU stay (in hours) for patients and the number of critical events they were exposed to per day (–0.09; 95% CI, –0.19 to 0.02; $p = 0.112$) after adjusting for the age, sex, and PRISM score of the patient at admission.

To further explore our observations, we determined the association between exposure to critical events and the initiation of noninvasive respiratory support interventions (high flow nasal cannula, continuous positive airway pressure or bilevel positive airway pressure) in other patients over the next 6 hours. In an unadjusted analysis, there was a modest increase in the risk of requiring noninvasive respiratory support for patients who were exposed to critical events compared with those were not (OR, 1.03; 95% CI, 1.00–1.06; $p = 0.02$). This association was no longer significant when adjusted for the number of patients in the ICU (OR, 1.00; 95% CI, 0.97–1.03; $p = 0.81$). Finally, we conducted an analysis of frequency of outcome for different exposure types. Of 24,909 observations where there was at least one exposure to the initiation of mechanical ventilation, the majority (24,785; 99%) did not result in an outcome for other patients in the next 6 hours. When there was an outcome observed in the next 6 hours ($n = 124$), it was most likely to be a mechanical ventilation event followed by the initiation of

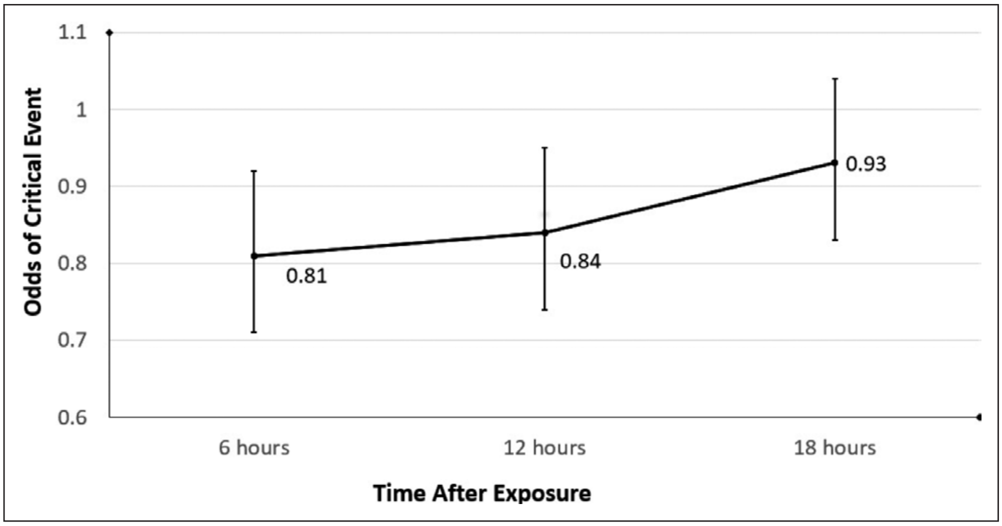

Figure 1. Association between exposure to critical events and patient outcome for different intervals of time. Data indicate a decrease in the risk of a critical event occurring in another patient which is most pronounced at 6 hr and gradually wanes over time to no longer significant at 18 hr.

TABLE 3.
Change in the Association Between Being Exposed to a Critical Event and Patient Outcome in the Next 6 Hours, Based on the Age of the Exposed Patient

Age (yr)	OR	95% CI
Overall	0.81	0.70–0.95
0–2	0.80	0.64–0.98
3–6	0.61	0.39–0.92
7–11	0.80	0.48–1.25
> 11	1.04	0.74–1.43

OR = odds ratio.

vasoactives (56% vs 22%). Similar observations were made for vasoactive exposure, where 63 of 13,583 observations resulted in an outcome in another PICU patient, and this outcome was most likely to be the initiation of mechanical ventilation (60%) and then vasoactives (27%). **Supplementary Table 2** (http://links.lww.com/CCX/B59) describes the result of these exposure-outcome pair comparisons.

DISCUSSION

In this retrospective study, we found that the occurrence of a critical event in the PICU is associated with a decrease in the odds of similar events occurring in other PICU patients within the next 6 hours by 19%, after adjusting for patient- and unit-level confounders. This association wanes over time and is no longer significant at 18 hours after exposure to a critical event. Last, the association varied by the age of the patient who was exposed. Younger patients experienced were less likely to experience a critical event after exposure compared with older patients, with no association seen in patients over 7 years old.

Few studies have explored the association between nonpatient factors and outcomes in pediatric patients. Increased provider workload has been shown to adversely affect patient outcomes in multiple settings (6, 7, 12). For example, in the study by Tubbs-Cooley et al (6), neonatal ICU nurses with higher workloads had a higher likelihood of reporting missed care for their patients. Another study by Fundora et al (7) concluded that PICU patients who were admitted when the unit had a higher occupancy rate and decreased staffing were found to have a higher mortality and longer length of stay. However, these studies did not consider the impact of critical events on patient outcomes. Our study fills this gap in knowledge and indicates that exposure to critical events is associated with decreased risk of events in other patients in the subsequent 6 hours. This is in direct contrast with the study by Volchenboum et al (8) in adult ward patients, which demonstrated that a single occurrence of a deterioration event increases the likelihood of a similar event in other ward patients by 19% within the next 12 hours. However, these observed differences may be explained by a few reasons. First, our study focuses on PICU patients who are cared for in settings that have a higher nurse to patient ratio and are generally better equipped to deal with critical events in comparison to an adult inpatient ward. For example, a recent cross-sectional study by McHugh et al (12) demonstrated that although adult ward patients had a higher risk of mortality after in-hospital cardiac arrest with increased workload for nurses, outcomes in patients in the ICU were not dependent on ICU nurse workload.

Thus, it is possible that hospital ICUs are more resilient to disruptive events. Second, the occurrence of a critical event in children might trigger a different response from caregivers than those in adults. Notably, we saw a 3% increase in the likelihood of non-invasive respiratory support interventions in an unadjusted analysis. Although these interventions may not decrease the risk of imminently needing vasoactive support or having a cardiac arrest, they may decrease the risk of requiring mechanical ventilation which was the most common critical event in our study. It is possible, then, that the sense of hypervigilance in the care team as a consequence of the rapid mobilization of resources in response to a critical event leads to improved care of patients in the PICU.

The detected association of decreased likelihood of a critical event for a patient when exposed to prior critical events within the ICU was observed at 6 and 12 hours and was null association otherwise. It is possible that after the occurrence of a critical event in the PICU, the care team focuses on stabilizing the patient before shifting attention to other PICU patients, potentially contributing to the change in association when increasing the time period from 4 to 6 hours. Additionally, there might be a lag time between care decisions made for other PICU patients and improvements in their health are observed. The association persists for at least 12 hours and was observed to decrease at 18 hours after an exposure event. This decrease may arise from several factors. First, as the exposure event becomes more remote, the healthcare team may return to baseline from their hypervigilant state. Second, it is possible that shift changes in personnel impact care, potentially altering the association; in this PICU, both attending physicians and bedside nurses change shifts approximately every 12 hours. Interestingly, we note that the association of critical events to our primary outcome changed with the age of the index patient. Younger patients had a lower risk of critical events, whereas there was no association when the age of the patient was more than 7 years. However, this could be related to the occurrence of fewer critical events in older children. Although we cannot rule out the possibility that the observed association might be of stochastic nature, the persistence of the association throughout sequential adjustment across the patient's length of stay, the time-varying nature of the association, and the observed increase in noninvasive interventions all point to the detection of a true association that needs be explored further through external validation and mechanistic studies.

To better understand the impact of critical events, we attempted to assess differences between overall ICU outcomes for patients who were exposed to critical events in comparison to patients who did not have any exposure throughout their ICU stay. Our analysis revealed that patients who were exposed had a significantly lower in-hospital mortality compared with others. There was no significant association between ICU length of stay and exposure to critical events. Thus, although a higher workload and ICU census increase the risk of mortality and a longer length of stay (7), our study indicates that the occurrence of critical events does not contribute to this increased risk. It is possible that ICU survivors would have a longer length of stay compared with nonsurvivors and therefore have a greater likelihood of being exposed to critical events. However, our analysis was not powered to further study the causal direction of this association. Further studies will be necessary to elucidate the interaction between these nonpatient factors and patient outcomes in the ICU.

There are several limitations to our study. First, this is a single-center study which may not be generalizable to other hospitals. Expanding to multicenter data will provide external validation, more granularity in terms of the number of and severity of exposure events, and a better understanding of this association in different settings. Second, the dataset used for this study did not differentiate between patients who were placed on mechanical ventilation after urgent intubation and those who were routinely placed on mechanical ventilation via tracheostomy tube. However, to minimize the number of nonurgent instances of mechanical ventilation and to exclude patients who are routinely ventilated at night, only patients who remained ventilated for at least 24 hours were counted as experiencing critical events. Our data also did not have information regarding physical locations of patients, thereby precluding a neighborhood-level analysis. Finally, given our relatively long study period, it is possible that changes in clinical practice, guidelines, unit structure, and logistics of in-house attending coverage might have occurred. Although our analysis demonstrated that adjusting for year did not change our main results, these factors may have an independent association with patient outcomes that is not well understood and may have an important bearing on the findings of this study.

CONCLUSIONS

In conclusion, our retrospective study has identified a novel association between critical events in PICU patients and decreased risk of similar events occurring in neighboring PICU patients. The detected association was found to change with time and patient age and may reflect increased vigilance or resilience on part of the care team in the immediate period after a critical event. Further studies establishing the causal mechanism behind this association are needed. Our study also illustrates the importance of studying nonpatient level factors to better understand outcomes in the ICU.

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