The Association Between Fever and Subsequent Deterioration Among Hospitalized Children With Elevated PEWS

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ABSTRACT

OBJECTIVES: To evaluate the association between fever and subsequent deterioration among patients with Pediatric Early Warning Score (PEWS) elevations to ≥4 to inform improvements to care escalation processes at our institution.

METHODS: We performed a cohort study of hospitalized children at a single quaternary children’s hospital with PEWS elevations to ≥4 between January 1, 2014 and March 31, 2014. Bivariable analysis was used to compare characteristics between patients with and without unplanned ICU transfers and critical deterioration events (CDEs) (ie, unplanned ICU transfers with life-sustaining interventions initiated in the first 12 ICU hours). A multivariable Poisson regression was used to assess the relative risk of unplanned ICU transfers and CDEs.

RESULTS: The study population included 220 PEWS elevations from 176 unique patients. Of those, 33% had fever (n = 73), 40% experienced an unplanned ICU transfer (n = 88), and 19% experienced CDEs (n = 42). Bivariable analysis revealed that febrile patients were less likely to experience an unplanned ICU transfer than those without fever. The same association was found in multivariable analysis with only marginal significance (adjusted relative risk 0.68; 95% confidence interval 0.45–1.01; P = .058). There was no difference in the CDE risk for febrile versus afebrile patients (adjusted relative risk 0.79; 95% confidence interval 0.43–1.44; P = .44).

CONCLUSIONS: At our institution, patients with an elevated PEWS appeared less likely to experience an unplanned ICU transfer if they were febrile. We were underpowered to evaluate the effect on CDEs. These findings contributed to our recognition that (1) PEWS may not include all relevant clinical factors used for clinical decision-making regarding care escalation and (2) further study is needed in this area.
Hospitalized children requiring an unplanned transfer to the ICU experience worse clinical outcomes than patients admitted directly to the ICU. To improve these outcomes, a bedside consult with a rapid response team (RRT) composed of ICU personnel is often incorporated into care escalation systems to facilitate early identification and intervention for patients outside the ICU at risk for deterioration. The use of RRTs is associated with reductions in hospital-wide mortality, codes and cardiopulmonary arrests outside of the ICU, and emergent, unplanned ICU transfers. To facilitate early RRT activation, early warning scores (illness severity scores based primarily on objective vital-sign data) are used in many care escalation systems as a trigger for RRT activation. These scores are widely used for the purpose of identifying children at risk for deterioration, although data supporting their effectiveness are weak.

One commonly used early warning score is the Brighton Pediatric Early Warning Score (PEWS) created by Monaghan in 2005. Authors of multiple single-center studies have reported potential benefits of using PEWS to identify hospitalized children at risk for deterioration. PEWS redirects care team members’ attention to patients who are at risk for a more in-depth evaluation of changes in the patient’s condition, empowering nurses to escalate care up the hierarchy of the care team, and providing standardized language when escalating care. However, there is conflicting evidence on the superiority of PEWS at identifying deterioration compared with provider intuition and clinical recognition, and care team members may not feel that acuity scores like PEWS are helpful in patients who are well appearing or those with abnormal physiology due to chronic underlying conditions. A recent large multisite randomized control trial revealed no improvement in mortality after the implementation of an early warning system in which a similar early warning score was used. Regardless, using PEWS as a trigger tool for RRT activation significantly increases the frequency of RRT activations and 1 study revealed that it led to increased resource use without improved patient outcomes.

During the study period, PEWS was used at our institution as a trigger for mandatory RRT activation whenever the score elevated to ≥4 (Fig 1). Compliance with this protocol was low at 40% to 60%, and care teams offered many reasons for why they did not feel RRT activation was indicated despite an elevated PEWS. One common explanation was the presence of fever as a physiologic cause of the elevated PEWS such that the score was not felt to be representative of impending deterioration. As many as 8% to 10% of hospitalized children have a documented temperature >38.0°C largely because fever is present in the majority of children with acute viral respiratory infections, which represent a significant proportion of hospitalized children. Serious bacterial infections also cause fever but are rare in children because only 3% of patients in the emergency department who are febrile have a urinary tract infection, 3% have pneumonia, and <1% have bacteremia. Regardless of etiology, fever can increase a child’s respiratory rate by 2.2 breaths per minute and can increase a child’s heart rate by 9.9 to 14.1 beats per minute with every 1°C rise in body temperature. As evident by the PEWS criteria outlined in Fig 1, changes in vital signs can significantly alter a patient’s PEWS. Consequently, care team members in certain circumstances may feel a PEWS is falsely elevated because of transient, physiologic vital sign changes in response to a fever rather than a more nefarious cause necessitating ICU interventions.

Our purpose for this study is to determine if there is an association between fever and subsequent deterioration among patients with an elevated PEWS at our institution. We hypothesize that hospitalized children who are febrile at the time of the PEWS elevation are less likely to be transferred to the ICU and to experience critical deterioration events (CDEs) (unplanned ICU transfers with life-sustaining interventions in the first 12 ICU hours) than children who are not febrile. To date, authors of no studies have evaluated these associations despite the frequent use of fever at our institution as a benign, physiologic explanation for PEWS elevations, justifying a lack of care escalation. With the results of this study, we will provide evidence as to whether our physicians are appropriately using the presence of fever in their clinical assessment of patients with an elevated PEWS. We will apply the findings to efforts to improve our local care escalation system because these results may inform discussions on provider behavior and the optimal use of PEWS within our broader care escalation system.

**METHODS**

This project was determined not to be human-subjects research and was approved for conduct by our institutional organizational research risk and quality improvement review panel.

**Study Design**

To inform our local care escalation system and culture, we sought to answer the following question: Among hospitalized children with PEWS elevations to ≥4 at our institution, are patients who are febrile at the time of the elevation less likely to experience unplanned ICU transfers and CDEs in the subsequent 12 hours than patients who are afebrile?

To best answer this question, we used a retrospective cohort study design to compare subjects with and without subsequent unplanned ICU transfers and CDEs. All subjects had PEWS elevations to ≥4.

**Data Source and Context**

Data collection was limited to hospitalized children at our primary children’s hospital. Our site is a quaternary care children’s hospital with on-site PICU and pediatric subspecialty services. During the study period, certain higher acuity interventions were permitted outside the ICU, including heated high-flow nasal cannula (HHFNC), continuous albuterol, and, if it was the patient’s established baseline respiratory support, positive pressure ventilation (PPV).

Clinical and demographic data were extracted from our electronic health record.
on all patients admitted to non-ICU, noncardiology, and nonpsychiatry units between January 1, 2014, and March 31, 2014, with PEWS elevations to $4. All hospitalizations were evaluated, including recurrent hospitalizations for the same patient. Multiple consecutive elevated PEWS on the same patient were combined into a single event for further analysis (Fig 2). The automated data were supplemented by a manual chart review performed by 3 of the study authors with expertise in this field.

**Measures**

Our primary explanatory variable was fever at the time of the PEWS elevation. This was defined as having a temperature $\geq 38.0^\circ C$ as the most recently documented temperature at or before the time of elevation. This was a dichotomous, categorical variable.

Our primary outcome was a subsequent unplanned ICU transfer after the PEWS elevation. This was defined as an ICU transfer within 12 hours of the time of elevation as documented in our electronic health record. This was a dichotomous, categorical variable.
Our secondary outcome was a subsequent CDE, defined by Bonafide et al.36 as an unplanned ICU transfer with a life-sustaining intervention in the first 12 hours in the ICU. On the basis of a review of the criteria by Bonafide et al.36 and consensus of the study team to resolve ambiguity, we characterized life-sustaining interventions as noninvasive ventilation (excluding high-flow nasal cannula), intubation, and vasopressor infusion. An event was characterized as a CDE if the unplanned ICU transfer happened within 12 hours of the PEWS elevation, and ≥1 of the listed life-sustaining interventions were initiated within 12 hours of the transfer. This secondary outcome was included to address the concern that our primary outcome, an unplanned ICU transfer, may in certain scenarios represent physician behavior rather than the patient’s true need for life-sustaining interventions.

Additional clinically relevant variables were considered as possible confounders for inclusion in the analysis (Table 1). To account for care team familiarity with the patient, we created a repeat events variable to control for potential differences between first-time events and repeat events. Because consecutive elevated PEWS on a single patient were grouped into a single event for analysis, these repeat events must be separated by time and include a PEWS <4 in the interim. The presence of an underlying complex chronic condition (CCC) was determined by using the CCC classification system by Feudtner et al.39 The patient’s primary admission diagnoses were collapsed into 3 clinically relevant groups by consensus of the research team: acute respiratory, oncologic, and other (composed primarily of neurologic diagnoses). A nighttime event was defined as a PEWS elevation that occurred between 9:00 PM and 9:00 AM to capture the perceived difficulty of behavior assessments overnight and the differences in our normal heart rate ranges when awake versus asleep.40 Age was stratified to <1 year and ≥1 year.

**Analysis**

A bivariable analysis was first used to compare clinical and demographic characteristics between those with and without unplanned ICU transfers and CDEs. Wilcoxon rank sum tests were used to compare median values of continuous variables, and χ² tests were used to compare proportions for categorical variables.

Age and sex were identified a priori for inclusion in the multivariable model because of their significant clinical relevance to the research question. Additionally, covariates with $P < .2$ on the bivariable analysis for unplanned ICU transfers and CDEs were considered in the respective multivariable models. The primary multivariable model for unplanned ICU transfers included all additional covariates with $P < .2$ in the multivariable analysis. The number of covariates permissible in the multivariable model for our sensitivity analysis was limited by the low number of events in our subject population,41 and only those deemed the most clinically relevant were included. For both models, covariates were evaluated for correlation, and, if present, the most clinically relevant variables were chosen for inclusion.

The multivariable analysis was performed by using Poisson regression with robust error variance to calculate adjusted relative risks (aRRs) and 95% confidence intervals (CIs), comparing the primary explanatory variable to the outcomes of interest after adjusting for covariates. Poisson regression with robust error variance was chosen because it allowed us to calculate relative risks (rather than odds ratios) with improved accuracy of the SE and CIs with increasing outcome incidence.42,43 Certain variables were identified on the basis of previous knowledge in the field as potential effect modifiers for the relationship between fever and both outcomes. These included age, primary diagnosis, HHFNC, and CCC. Because of restrictions in sample size, we tested these interactions using Zelen’s exact test (an exact test version of the Cochran-Mantel-Haenszel test) for multiway 2-by-2 tables rather than in multivariable models.

**RESULTS**

The study population included 220 unique PEWS elevation events, none of which were excluded (Fig 2). Of the 220 PEWS elevations, 40% required an unplanned ICU transfer, and 19% experienced a CDE in the subsequent 12 hours. The population was composed of patients admitted to the following services: general pediatrics and other medical subspecialties (51.4%); hematology, oncology, and bone marrow transplant (27%); pulmonology (16%); and surgical services and inpatient rehabilitation (6%). Additional patient and clinical event characteristics are shown in Table 1.

**Bivariable Analysis**

Bivariable comparisons are shown in Table 2. For patient-specific characteristics
expected to remain constant throughout the study period (age, sex, CCCs, and chronic dependence on PPV), comparisons were performed by using only the first event for each individual patient \((n = 176)\). For all other characteristics, the full study population was used for the bivariable analysis \((N = 220)\).

**Final Multivariable Models**

Total PEWS, the PEWS subset scores, and change from the previous PEWS were highly correlated, and total PEWS was chosen for inclusion in the model because of both its statistical significance in the bivariable analysis and its clinical relevance. On the basis of the results of the bivariable analysis, our final multivariable model for our primary analysis of unplanned ICU transfers included the following covariates: presence of fever, age, sex, repeat patient, CCCs, primary diagnosis, total PEWS, and acute dependence on HHFNC. The final multivariable model for our secondary analysis of CDEs was limited to the following covariates: presence of fever, age, sex, total PEWS, and HHFNC. Of the variables with \(P < .2\) on the bivariable analysis of CDEs, HHFNC and total PEWS were chosen for inclusion in our multivariable model because of their clinical relevance to the study question.

**Multivariable Analysis**

Results of the multivariable analyses are shown in Fig 3.

Our primary analysis revealed with marginal significance that patients with fever at the time of the PEWS elevation were 32\% less likely than those without fever to experience an unplanned ICU transfer in the subsequent 12 hours \((aRR 0.68; 95\% CI 0.45–1.01; P = .058)\). Patients acutely dependent on HHFNC were 57\% more likely than patients not requiring HHFNC \((aRR 1.57; 95\% CI 1.15–2.13; P = .004)\), and boys were 27\% less likely than girls to experience an unplanned ICU transfer in the subsequent 12 hours \((aRR 0.73; 95\% CI 0.54–0.996; P = .047)\). Additionally, the risk of a subsequent unplanned ICU transfer went up 40\% with every 1-point increase in total PEWS \((aRR 1.40; 95\% CI 1.23–1.59; P < .0001)\). The aRR was not statistically significant for all other variables in the primary model.

Our secondary analysis did not reveal a statistically significant risk of CDEs based on the presence or absence of fever at the time of a PEWS elevation \((aRR 0.79; 95\% CI 0.43–1.44; P = .44)\). The risk of a CDE in the subsequent 12 hours after a PEWS elevation went up 50\% with every 1-point increase in total PEWS \((aRR 1.50; 95\% CI 1.19–1.89; P = .001)\). The aRR was not statistically significant for all other variables in the secondary model.

**Assessment of Effect Modification**

The analysis of potential effect modifiers did not yield statistically significant results, although the primary diagnosis approached significance \((P = .068)\). Among subjects with a respiratory diagnosis, the odds of having a CDE for subjects with fever (versus those without) was noticeably higher than in the other 2 diagnosis groups.

**DISCUSSION**

Children hospitalized at our institution who had fever at the time of a PEWS elevation were less likely than patients without fever to experience an unplanned ICU transfer in the subsequent 12 hours after a PEWS elevation to \(\geq 4\), although this association was only marginally significant, with a \(P\) value slightly above the traditional \(\alpha\) value of .05. This trend may support anecdotal reports that the inclusion of fever in decision-making regarding care escalation for patients with an elevated PEWS may have merit. Because we were underpowered to demonstrate the effect of fever on subsequent CDEs, we do not know to what degree these associations reflect the...
provider’s behavior and/or preferences versus the patient’s true need for ICU interventions. However, we do feel that an ICU transfer offers clinical benefits to patients with deteriorating conditions (eg, smaller nursing ratios, continuous monitoring, experienced personnel) even in the absence of life-sustaining interventions as defined by CDEs. Thus, our results may most accurately be represented as follows: among children with an elevated PEWS, those with fever appeared less likely to require an ICU transfer than those without fever. Such a conclusion has implications for resource use born from the potential overcalling of deterioration by an incomplete illness severity score.

A review of the remaining analysis revealed that the risk of experiencing an unplanned ICU transfer was higher if patients were acutely dependent on HHFNC than if they were not. This is not surprising because these patients are already experiencing respiratory failure and are often requiring the maximum allowable respiratory support outside of the ICU at our institution. Any signs of continued distress may represent the need for higher levels of respiratory support that can only be instituted in the ICU.

Our results also revealed that the risk of both unplanned ICU transfers and CDEs increased as PEWS increased, even after adjusting for confounders. These results suggest PEWS may have predictive value generally, although all relevant inputs may not be considered in the score for reliable use on individual patients. Thus, the ability to predict the need for care escalation with PEWS may vary significantly across different clinical scenarios. For example, 2 patients whose PEWS are elevated because of tachycardia may have significantly different risks of deterioration if 1 is febrile and the other is not. In that way, with our study, we may begin to offer care teams at our institution the ability to make more informed decisions at the point of care by offering evidence on the impact of fever on both PEWS and patient outcomes. This evidence should then be part of bedside discussions with patients with a high PEWS.

Further study is needed. An adequately powered study used to evaluate the association between additional clinical factors and patient outcomes in this population would contribute to the improvement of the current PEWS and

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**TABLE 2** Bivariable Analysis Used to Compare Characteristics Between Events With and Without Unplanned ICU Transfers and CDEs in the 12 Hours After a PEWS Elevation

<table>
<thead>
<tr>
<th>Variable</th>
<th>No ICU Transfer</th>
<th>ICU Transfer</th>
<th>P</th>
<th>No CDE</th>
<th>CDE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population, n (%)</td>
<td>132 (100)</td>
<td>88 (100)</td>
<td>N/A</td>
<td>178 (100)</td>
<td>42 (100)</td>
<td>N/A</td>
</tr>
<tr>
<td>First event only, n (%)</td>
<td>100 (76)</td>
<td>76 (86)</td>
<td>N/A</td>
<td>141 (79)</td>
<td>35 (83)</td>
<td>N/A</td>
</tr>
<tr>
<td>Repeat event, n (%)</td>
<td>32 (24)</td>
<td>12 (14)</td>
<td>.054</td>
<td>37 (21)</td>
<td>7 (17)</td>
<td>.548</td>
</tr>
<tr>
<td>Age, y, n (%)</td>
<td></td>
<td></td>
<td>.038</td>
<td>.984</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>17 (17)</td>
<td>23 (30)</td>
<td></td>
<td>32 (23)</td>
<td>8 (23)</td>
<td></td>
</tr>
<tr>
<td>≥1</td>
<td>83 (83)</td>
<td>53 (70)</td>
<td></td>
<td>109 (77)</td>
<td>27 (77)</td>
<td></td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td>.060</td>
<td>.186</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>59 (59)</td>
<td>34 (45)</td>
<td>78 (55)</td>
<td>15 (43)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>41 (41)</td>
<td>42 (55)</td>
<td>63 (45)</td>
<td>20 (57)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDC, n (%)</td>
<td>50 (50)</td>
<td>29 (38)</td>
<td>.118</td>
<td>63 (45)</td>
<td>16 (46)</td>
<td>.912</td>
</tr>
<tr>
<td>Chronic PPV dependence, n (%)</td>
<td>8 (8)</td>
<td>7 (9)</td>
<td>.776</td>
<td>9 (6)</td>
<td>6 (17)</td>
<td>.082</td>
</tr>
<tr>
<td>Primary diagnosis category, n (%)</td>
<td></td>
<td></td>
<td>.016</td>
<td>.285</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>61 (46)</td>
<td>61 (69)</td>
<td>93 (52)</td>
<td>29 (69)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncologic</td>
<td>38 (29)</td>
<td>12 (14)</td>
<td>45 (23)</td>
<td>5 (12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td>6 (5)</td>
<td>2 (2)</td>
<td>6 (3)</td>
<td>2 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonrespiratory infection</td>
<td>9 (7)</td>
<td>4 (5)</td>
<td>11 (6)</td>
<td>2 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>18 (14)</td>
<td>9 (10)</td>
<td>23 (13)</td>
<td>4 (10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fever, n (%)</td>
<td>53 (40)</td>
<td>20 (23)</td>
<td>.008</td>
<td>61 (34)</td>
<td>12 (29)</td>
<td>.540</td>
</tr>
<tr>
<td>Total PEWS, median (IQR)</td>
<td>4.0 (4.0–4.0)</td>
<td>4.0 (4.0–5.0)</td>
<td>.002</td>
<td>4.0 (4.0–5.0)</td>
<td>4.0 (4.0–5.0)</td>
<td>.086</td>
</tr>
</tbody>
</table>

**PEWS subset scores, median (IQR)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No ICU Transfer</th>
<th>ICU Transfer</th>
<th>P</th>
<th>No CDE</th>
<th>CDE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behavior</td>
<td>1.0 (0.0–1.0)</td>
<td>1.0 (1.0–1.0)</td>
<td>.162</td>
<td>1.0 (0.0–1.0)</td>
<td>1.0 (1.0–1.0)</td>
<td>.224</td>
</tr>
<tr>
<td>Respiratory</td>
<td>2.0 (1.0–3.0)</td>
<td>2.0 (2.0–3.0)</td>
<td>&lt;.001</td>
<td>1.0 (1.0–2.0)</td>
<td>1.0 (0.0–1.0)</td>
<td>.005</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>2.0 (1.0–2.0)</td>
<td>1.0 (1.0–1.5)</td>
<td>.001</td>
<td>2.0 (1.0–3.0)</td>
<td>3.0 (2.0–3.0)</td>
<td>.002</td>
</tr>
<tr>
<td>Change from previous PEWS, median (IQR)</td>
<td>2.0 (1.0–3.0)</td>
<td>2.0 (1.0–3.0)</td>
<td>.959</td>
<td>2.0 (1.0–3.0)</td>
<td>2.0 (1.0–3.0)</td>
<td>.458</td>
</tr>
<tr>
<td>Acute HHFNC, n (%)</td>
<td>25 (19)</td>
<td>36 (41)</td>
<td>&lt;.001</td>
<td>46 (26)</td>
<td>15 (36)</td>
<td>.199</td>
</tr>
<tr>
<td>Continuous albuterol, n (%)</td>
<td>11 (8)</td>
<td>8 (9)</td>
<td>.845</td>
<td>16 (9)</td>
<td>3 (7)</td>
<td>&gt;.999</td>
</tr>
<tr>
<td>Nighttime event, n (%)</td>
<td>80 (45)</td>
<td>39 (44)</td>
<td>.868</td>
<td>80 (45)</td>
<td>19 (45)</td>
<td>.972</td>
</tr>
</tbody>
</table>

IQR, interquartile range; N/A, not applicable.
creation of a novel illness severity score better equipped to guide clinical decision-making regarding deterioration.

Our study has limitations. First, it is important to consider that although the aRR used to compare fever to unplanned ICU transfers in the multivariable analysis was marginally significant, and the upper confidence limit crossed 1. Second, the study population was obtained during the winter (“respiratory season”), and 56% of subjects had an acute respiratory infection. Because a temperature >38.0°C is an expected part of the natural course of illness in viral respiratory infections, these patients may be overrepresented among our cohort of patients with fever. Third, our interaction analyses did not reveal any statistically significant effect modifications between the chosen covariates and fever in relation to our outcomes, but further study with a larger sample size would allow for better assessment of these interactions. Finally, the study population was drawn from a single institution in 2014. However, PEWS has not changed at our institution since 2014, and care team members’ perceptions of the associations between PEWS and fever have also remained constant. The data were collected for process improvement purposes, and results do not represent generalizable knowledge.

CONCLUSIONS

At our institution, patients with fever at the time of a PEWS elevation may be less likely to experience an unplanned ICU transfer than patients without fever. We were underpowered to detect significant differences in CDEs and, therefore, do not know the degree to which this association represents provider behavior versus true differences in patient deterioration. Nonetheless, fever is likely one of many clinical variables that can confound the interpretation of PEWS, limiting its utility as a stand-alone trigger tool for care escalation.

REFERENCES


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