Use of white cell count, age, and presence of other injuries in stratifying risk of intracranial injury in pediatric trauma

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ABSTRACT

The Pediatric Emergency Care Applied Research Network (PECARN) Head Injury/Trauma Algorithm is a well-validated decision rule used to identify patients at low risk of clinically important traumatic brain injuries who may not need head CT. In adult patients with mild head trauma, elevated serum glucose and white cell count (WCC) have been associated with abnormal head CT findings. Currently, glucose or WCC is not considered in pediatric patients. The objective of this study was to determine if elevations in glucose or WCC could be used as additional tools to risk-stratify pediatric trauma patients for intracranial injury (ICI). Data were abstracted from the Maryland Trauma Registry and from electronic medical records for patients at the Johns Hopkins Children's Center from 2017 to 2020. We evaluated 145 encounters that met the inclusion criteria. There were 33 cases of ICI on CT. In addition to higher median glucose and WCC, we found that patients with ICI had a younger median age and were less likely to have other clinically significant injuries than patients without ICI. Following multiple logistic regression analysis, WCC (OR 1.113, 95% CI 1.02 to 1.21), younger age (OR 0.89, 95% CI 0.8 to 0.98), and absence of other injuries (OR 0.41, 95% CI 0.23 to 0.73) were found to be associated with risk of ICI. The area under the curve for our model was 0.79. When used with the PECARN algorithm, our model could help determine which patients may avoid head CT or undergo a shorter observation period.

INTRODUCTION

Emergency departments (ED) are faced with the challenge of assessing intracranial injury (ICI) in pediatric trauma patients in 600,000 visits annually in the USA.[1] While a useful diagnostic tool, CT imaging carries a non-negligible and well-documented risk of future malignancy in children due to radiation exposure. Miglioretti *et al*[2] found that the 4 million pediatric CT scans performed each year in the USA were estimated to cause 4870 future malignancies. For head imaging, they found the risk of leukemia to be 1.9 per 10,000 scans.[2] Although radiation-induced malignancy in children is a small contribution to overall cancer mortality, the risk warrants that CT only be used when there is a high index of suspicion for injury.

The Pediatric Emergency Care Applied Research Network (PECARN) Pediatric Head Injury/Trauma Algorithm is a well-validated clinical decision aid that allows physicians to safely identify patients at low risk of clinically important traumatic brain injuries (ciTBI) without the need for CT imaging. Kuppermann *et al*[1] found that ciTBIs, as well as evidence of ICI on CT, were rare in children. Yet head CTs were obtained in up to 35% of patients, likely underestimating the national average of 50%.[1] The PECARN algorithm recommends a CT scan for high-risk patients and no CT scan for low-risk patients.[1] For intermediate-risk patients, there is no definitive recommendation. The decision as to whether these patients undergo CT or upwards of 6 hours of observation relies on physician experience, parental preference, multiple versus isolated findings, and worsening symptoms.[1] Due to the mechanism, many patients who are passengers in motor vehicle collisions (MVC) or who are struck by motor vehicles are stratified into the intermediate-risk category. This population, however, makes up a small proportion (13%) of the PECARN cohort relative to falls.[1] Falls, the most common cause of non-fatal unintentional injury in the USA in children aged 0–19, account for over 50% of the PECARN algorithm's injury mechanisms.[1,3]

Trauma is a known cause of systemic inflammatory response syndrome, which is defined hematologically by a white cell count (WCC) above 12 $\times 10^9$/L, below 4 $\times 10^9$/L or 10% bands.[4] Leukocytosis following trauma is a well-established occurrence. Bodhit *et al*[5] reported that elevated serum glucose and WCC predicted abnormal CT findings in adult patients with mild head trauma. Currently, serum glucose or WCC is not considered in the PECARN algorithm in determining the risk of ICI. Therefore, the primary objective of this study was to assess the relationship of glucose and WCC with the presence of ICI in pediatric trauma. The secondary objective was to assess other variables that may also be associated with the presence of ICI, especially in patients with multi-trauma.

METHODS

Study design

This was a single-center retrospective study of pediatric trauma patients seen at the Johns Hopkins Children's Center (JHCC) from January 2017 to July 2020. JHCC is a pediatric quaternary care referral center and a level I trauma center in Baltimore, Maryland, with an annual census of 35,000. Patients with confirmed ICI on CT were identified by screening patients from the Maryland Trauma Registry who had both a head CT and a neurosurgery consult placed in the ED. All other trauma patients were selected by reviewing randomly generated medical record numbers sequentially for inclusion and exclusion criteria. We abstracted data from the electronic medical record. The primary outcome variable was the presence of ICI, defined as an intracranial injury, including skull fracture, identified by radiography, or absence of ICI, as determined by negative imaging or lack of clinical worsening during an observation period of 4–6 hours in the ED. Our study included pediatric trauma patients under the age of 18 who had labs drawn in the ED. We excluded patients (1) in cardiac arrest or in peri-arrest, (2) with documented signs or history of recent bacterial or viral infections, (3) on steroids or immunosuppression, (4) with metabolic disorders, (5) with known bleeding disorders, and (6) seen after drowning. A waiver of informed consent was granted due to the retrospective nature of the review and use of deidentified data.

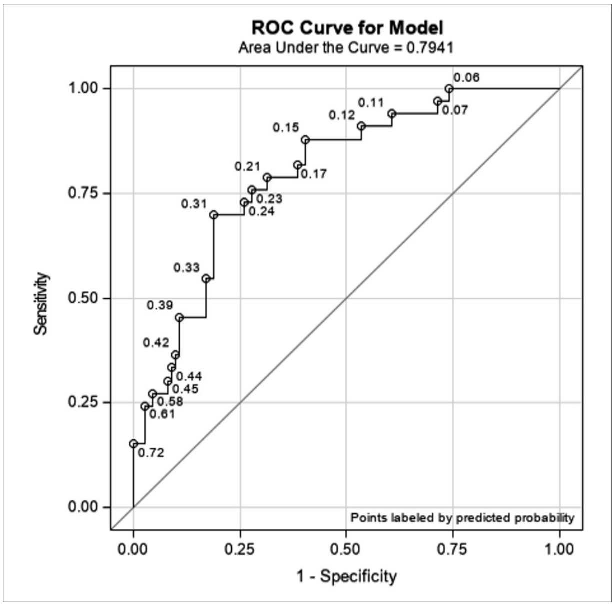

Figure 1 Receiver operating characteristic (ROC) curve for white cell count, age, and absence of other injuries as predictive factors of intracranial injury. True positive rate is plotted along the y-axis and false positive rate is plotted along the x-axis. Each data point is labeled with the predicted probability threshold.

Statistical analysis

We set $p<0.05$ as our threshold for significance. We chose a study population of 145 patients to achieve 81.4% power to detect a difference of 3 $x10^9$/L in WCC. Frequencies, percentages, medians, and IQR were calculated to describe the population. We compared patients with ICI with patients with no ICI using Wilcoxon rank-sum tests for continuous variables and Fisher's exact tests for categorical variables. Multiple logistic regression analysis was used to identify predictors of ICI. Performance characteristics of our model were evaluated by plotting the true positive and false positive rates to generate a receiver operating characteristic (ROC) curve. The ROC curve for our model displays an area under the curve of 0.79 (figure 1). We evaluated several models with WCC and age dichotomized (WCC cut-off of 10 or median of 10.96; age cut-off of 2 or 9), or natural log-transformed, and found the model with linear age and WCC to have the best fit (Hosmer-Lemeshow goodness of fit $\chi^2=1.49$, $p=0.99$) and diagnostics.

RESULTS

There were 145 patients who met the inclusion criteria; 33 had ICI. Of the 33 patients, 19 were determined to be high risk and 14 were determined to be intermediate risk, as defined by the PECARN algorithm. Of the 33 patients with ICI, 27 (81.8%) had no secondary injuries. We analyzed the 112 patients with no ICI, of whom 53 had clinically significant injury and 59 had no injury identified, as one group. Clinically significant injuries were defined as maxillofacial fractures, extremity fractures, intrathoracic injuries, or intra-abdominal injuries. Falls occurred more frequently in patients with ICI than in patients with no ICI (42% vs 18%), and patients with no ICI were more frequently passengers in MVC than patients with ICI (21% vs 12%) (table 1). Patients with ICI had a younger median age, higher median WCC, higher median glucose, and lower rate of other clinically significant injury than patients with no ICI (table 1). Glucose was not statistically associated with risk of ICI. The three predictors of ICI in our multiple logistic regression model were elevated WCC, younger age, and absence of other injuries. WCC predicted ICI with an OR of 1.113 (95% CI 1.02 to 1.21), age with an OR of 0.89 (95% CI 0.8 to 0.98), and other injuries with an OR of 0.41 (95% CI 0.23 to 0.73).

DISCUSSION

In this study, we found elevated WCC, younger age, and absence of other clinically significant injury to be predictive of ICI. We are not suggesting, however, that these factors are a stand-alone means of stratifying patients at risk of ICI. In conjunction with the PECARN algorithm, these factors may help determine which patients with minor head trauma are at low risk of ICI and can avoid CT or a prolonged ED observation. While PECARN algorithm factors such as physician experience and parental preference are important in determining which intermediate-risk patients should undergo CT, having objective data points is crucial in an ED where the need for a rapid diagnosis may encourage the use of CT, with its risk of future malignancy. It is also crucial in an ED setting, where uncertainties in head trauma diagnosis may require 4–6 hours of observation, potentially limiting resources for other patients. Our study suggests that WCC, age, and absence of other injury can provide a model to help further stratify patients currently classified as intermediate risk by the PECARN algorithm.

To further understand the predictive power of younger age and absence of other injury, it is useful to compare

Table 1 Patient characteristics by presence or absence of intracranial injury

Characteristics	Presence of intracranial injury (n=33) Median (IQR)	Absence of intracranial injury* (n=112) Median (IQR)	P value
Age (years)	5 (2–9)	9.5 (5–13)	0.0014
WCC (×10^9/L)	14.77 (11.2–18.3)	10.02 (7.6–13.9)	0.00064
Glucose (mg/dL)	128 (105–148)	111 (99–136)	0.021
	%	%	
Presence of other injury	18.2	47.3	0.0027
Mechanism of injury			0.0141
Fall	42.4	17.9	
Struck by motor vehicle	39.4	40.2	
Passenger in motor vehicle collision	12.1	20.5	
Struck by another person/object	6.0	8.0	
Other	0	13.4	
Male gender	60.6	61.6	0.917
Race			0.123
White	57.6	34.8	
Black	30.3	48.2	
Other†	12.1	17.0	
Hispanic ethnicity	6.1	10.7	0.737

*Includes patients with no injury identified, skin/soft tissue injury, facial bone fracture, fractures of the pelvis or other extremity, intra-abdominal injury, spinal cord/vertebral body injury, and intrathoracic injury including rib fractures.
†Other race includes Asian, American Indian, mixed race, and not applicable.
WCC, white cell count.

these factors in our study with the factors in the PECARN algorithm. In our study, patients with ICI were significantly younger, with a median age of 5 years vs 9.5 years (p=0.0014), than those with no ICI (table 1). Similarly, the PECARN algorithm found the risk of head injury to be higher in younger children, with a rate of 0.9% for children <2 years old and 0.8% in children ≥2 years old.[1] Our model supports having a higher index of suspicion for ICI in children <2 years old, with possible extension to younger school-aged children.

Our finding that the presence of secondary injuries may decrease the risk of ICI suggests that the mechanism of trauma is important to consider. In our study, isolated head trauma occurred in 81.8% of patients, comparable with 90% of the PECARN cohort.[1] Of our patients with isolated head trauma, 52% sustained falls, 33% were struck by a motor vehicle, and 7% were passengers in an MVC. While initially counterintuitive, we hypothesize that the presence of secondary injuries could be indicative of blunt force trauma distributed to other regions of the body rather than localized to the head. In our study, the most common secondary injury was fracture of the extremities.

Our study has several strengths. Compared with the PECARN study, our study has a higher proportion of traumas from MVCs (19% vs 9%) and from being struck by a motor vehicle (40% vs 4%).[1] Because our model reflects a higher proportion of these trauma mechanisms, which are often classified as intermediate risk, our study provides additional information that may supplement the PECARN algorithm in risk-stratifying these mechanisms for the presence of ICI. For comparison, the area under the ROC curve for the PECARN algorithm is 0.81, compared with 0.79 for our model (figure 1).[6] Used in conjunction with the PECARN algorithm, our model may strengthen the algorithm's ability to identify intermediate-risk patients at low risk of ICI so they may avoid CT or a long ED observation. Considering the high volume of pediatric head trauma ED visits, the impact on resource utilization is not insignificant.

Our study also has some limitations. We acknowledge that we examined a small sample of patients with ICI. However, Kuppermann *et al*'s[1] study, the largest trial of its kind, also had low rates of ICI. Additionally, we only reviewed charts from the JHCC. As a quaternary care center, JHCC may receive more severe trauma cases than other centers, limiting the generalizability of our results. As a retrospective chart review, we are limited to the data recorded in the electronic medical record.

Our study presents a model for identifying which intermediate-risk patients are at low risk of ICI. When used with the PECARN algorithm, the model may distinguish intermediate-risk patients who can avoid CT exposure or undergo a shorter observation period. Ultimately, it has the possibility to reduce the risk of radiation-induced malignancy and better allocate resources in crowded EDs. In the future, we would like to examine if WCC, age, and isolated head injury continue to be statistically significant factors in a larger cohort through evaluation of ED visits before January 2017 and expanding to include multiple pediatric trauma centers. In addition, our finding that secondary injuries decrease the likelihood of ICI warrants more in-depth investigation.

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