Original Investigation

Clinical Risk Score for Persistent Postconcussion Symptoms Among Children With Acute Concussion in the ED

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IMPORTANCE Approximately one-third of children experiencing acute concussion experience ongoing somatic, cognitive, and psychological or behavioral symptoms, referred to as persistent postconcussion symptoms (PPCS). However, validated and pragmatic tools enabling clinicians to identify patients at risk for PPCS do not exist.

OBJECTIVE To derive and validate a clinical risk score for PPCS among children presenting to the emergency department.

DESIGN, SETTING, AND PARTICIPANTS Prospective, multicenter cohort study (Predicting and Preventing Postconcussive Problems in Pediatrics [5P]) enrolled young patients (aged 5-<18 years) who presented within 48 hours of an acute head injury at 1 of 9 pediatric emergency departments within the Pediatric Emergency Research Canada (PERC) network from August 2013 through September 2014 (derivation cohort) and from October 2014 through June 2015 (validation cohort). Participants completed follow-up 28 days after the injury.

EXPOSURES All eligible patients had concussions consistent with the Zurich consensus diagnostic criteria.

MAIN OUTCOMES AND MEASURES The primary outcome was PPCS risk score at 28 days, which was defined as 3 or more new or worsening symptoms using the patient-reported Postconcussion Symptom Inventory compared with recalled state of being prior to the injury.

RESULTS In total, 3063 patients (median age, 12.0 years [interquartile range, 9.2-14.6 years]; 1205 [39.3%] girls) were enrolled (n = 2006 in the derivation cohort; n = 1057 in the validation cohort) and 2584 of whom (n = 1701 [85%] in the derivation cohort; n = 883 [84%] in the validation cohort) completed follow-up at 28 days after the injury. Persistent postconcussion symptoms were present in 801 patients (31.0%) (n = 510 [30.0%] in the derivation cohort and n = 291 [33.0%] in the validation cohort). The 12-point PPCS risk score model for the derivation cohort included the variables of female sex, age of 13 years or older, physician-diagnosed migraine history, prior concussion with symptoms lasting longer than 1 week, headache, sensitivity to noise, fatigue, answering questions slowly, and 4 or more errors on the Balance Error Scoring System tandem stance. The area under the curve was 0.71 (95% CI, 0.69-0.74) for the derivation cohort and 0.68 (95% CI, 0.65-0.72) for the validation cohort.

CONCLUSIONS AND RELEVANCE A clinical risk score developed among children presenting to the emergency department with concussion and head injury within the previous 48 hours had modest discrimination to stratify PPCS risk at 28 days. Before this score is adopted in clinical practice, further research is needed for external validation, assessment of accuracy in an office setting, and determination of clinical utility.

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Concussion is a serious public health epidemic.[1,2] Rates have doubled during the last decade[3] with an estimated 750 000 pediatric acute concussion visits to emergency departments (EDs) occurring annually in the United States.[1,4] Although many children experience symptom resolution within 2 weeks, approximately 33% experience ongoing somatic, cognitive, psychological, behavioral symptoms, or a combination of these symptoms.[5,6] Symptoms persisting beyond 28 days are referred to as persistent postconcussion symptoms (PPCS)[7] and can have serious adverse effects, resulting in school absenteeism, impaired academic performance, depressed mood, loss of social activities, and lower quality of life.[8]

Validated and pragmatic tools to identify children at high risk of developing PPCS do not exist.[9] Adolescent age, female sex, and physician-diagnosed history of migraine have been associated with PPCS in children[5,10]; however, prior studies have had significant limitations. Retrospective studies are limited by poor data quality, missing data, minimal use of validated symptom scoring scales, and lack of standardized acute evaluation.[5,6,9-11]

Additional limitations include small sample sizes,[6,12] recruitment beyond the acute injury period,[13,14] and inconsistent definition and measurement of PPCS.[9] Studies including elite adolescent athletes and adults dominate the literature, limiting applicability to subsets of children. The Institute of Medicine and the National Research Council emphasized the need for a large, prospective study to quantify PPCS risk in children and youth and to establish "objective, sensitive, and specific metrics and markers of concussion diagnosis, prognosis, and recovery in youth."[15]

The Predicting and Preventing Postconcussive Problems in Pediatrics (5P) study was designed to derive and validate a clinical risk score to stratify PPCS risk occurring after acute concussion in children and youth using readily available clinical features.

Methods

Study Design

The 5P was a prospective, multicenter cohort study.[16] Participants were recruited from 9 pediatric emergency departments within the Pediatric Emergency Research Canada (PERC) network. Enrollment occurred from August 2013 through September 2014 (derivation cohort) and from October 2014 through June 2015 (validation cohort) (**Figure 1**). The study complied with the transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD) statement[17] and was approved by the ethics committees of the PERC participating institutions. Written consent and assent was obtained from all participants and their parents or guardians as appropriate. The trial protocol appears in Supplement 1.

Study Population

Eligible patients were aged 5 years through younger than 18 years, presented to a participating ED with a head injury within the preceding 48 hours, and met concussion diagnostic criteria consistent with the fourth Zurich consensus statement.[18] Concussion was defined as a complex pathophysiological process caused by a direct blow to the head, face, neck, or elsewhere on the body with an impulsive force transmitted to the head (which may or may not have involved loss of consciousness), resulting in a brain injury with 1 or more symptoms in 1 or more of the following clinical domains: somatic, cognitive, emotional or behavioral, or sleep (eTable 1 in Supplement 2).[18] Patients were excluded for (1) a Glasgow Coma Scale score of 13 or less, (2) a structural abnormality on neuroimaging (if performed), (3) a neurosurgical intervention, (4) intubation or intensive care unit admission, (5) multisystem injury requiring hospitalization, (6) procedural sedation, (7) severe preexisting neurological developmental delay resulting in communication difficulties, (8) intoxication, (9) absence of trauma as primary event, (10) previously enrolled in this same study, (11) insurmountable language barrier, or (12) the inability to follow-up by telephone or email.

Study Protocol

Procedures were identical for the derivation and validation phases of the study. Prior to study initiation, participating site ED physicians and research staff were trained on data collection methods using standardized training sessions during site visits by the principal investigator and the national coordinator. Trained research assistants completed standardized assessments of all patients as described in the published protocol.[16] Data were collected and managed using research electronic data capture.[19]

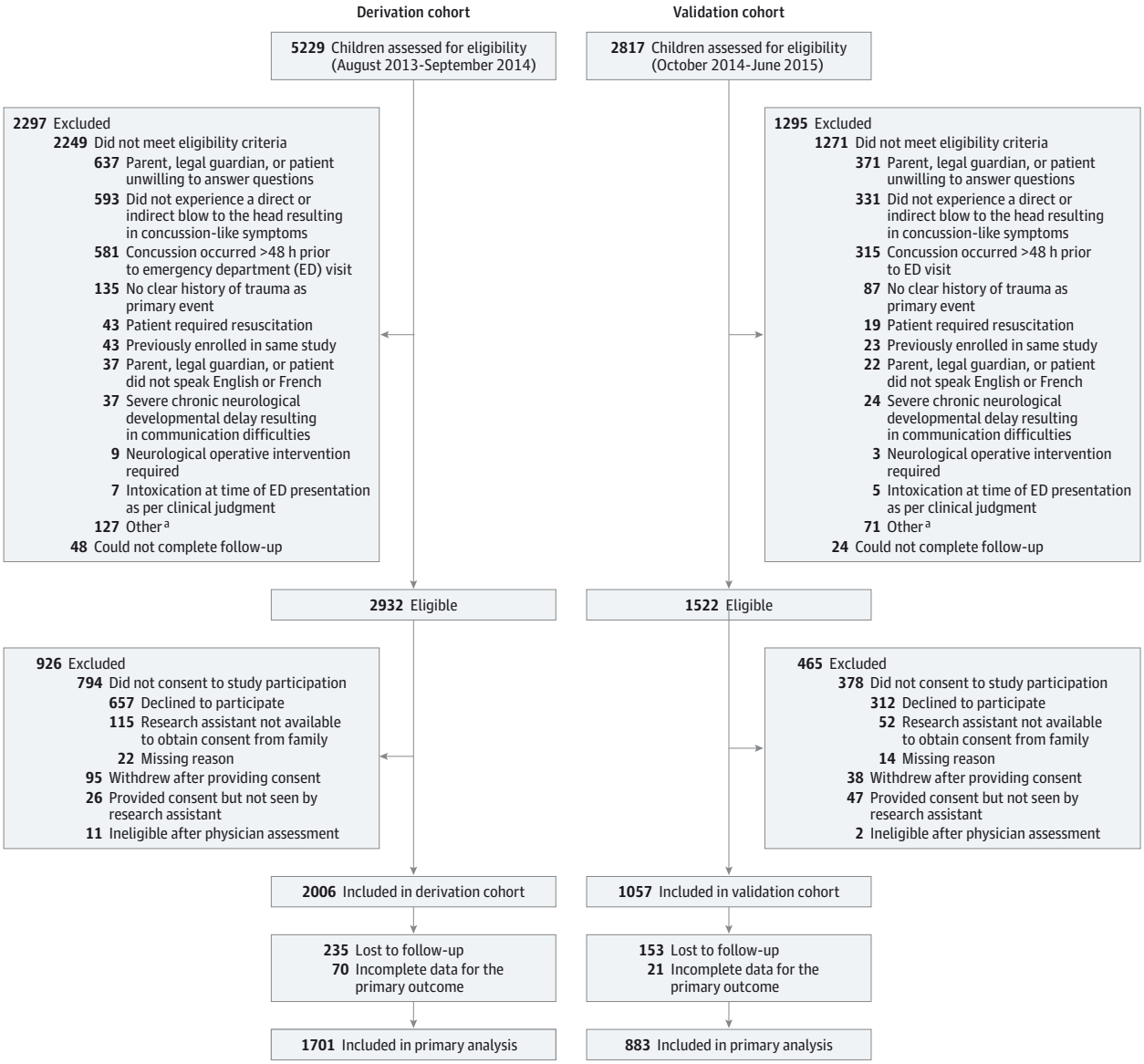
Patients and parents provided information on demographics, history, and injury characteristics using the Acute Concussion Evaluation inventory.[20] Patients and parents quantified state of being prior to the injury and current symptoms using the Postconcussion Symptom Inventory (eFigure 1 in Supplement 2).[21,22] Cognition, physical examination, and balance were assessed using the third edition of the Child-Sport Concussion Assessment Tool.[23] At enrollment, concussion; developmental, neurological, and psychiatric history; therapies received during the ED visit; discharge instructions; and treating physician prognostication of PPCS risk with predicted symptom duration were prospectively collected. Blinded, independent second raters in a convenience subset of 10% of patients duplicated data collection to assess reliability.[24]

Participants completed electronic follow-up surveys at 7, 14, and 28 days after the injury, including the patient-reported Postconcussion Symptom Inventory[16]; electronic capture was not expected to affect reporting.[25] Patients opting for web-based follow-up received email reminders 24 hours following each survey deadline; research assistants telephoned nonresponders and those opting for telephone follow-up up to 5 times to complete measures orally.

Primary Outcome Measure

The primary outcome measure, PPCS, was defined in keeping with the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)* definition of postconcussion syndrome, which requires persistence be-

Figure 1. Flow Diagram of Patients



[a] The research ethics board for 1 of the 9 sites did not permit the collection of reasons for meeting exclusion criteria due to provincial regulations. Therefore, the total for "other" includes not specified along with missing.

yond 4 weeks of at least 3 symptoms compared with state of being prior to the injury.[26] In the study, an individual symptom was defined as a positive difference between the patient-reported current minus the perceived preinjury symptom rating; both were completed 28 days after the injury.[26]

Secondary Outcome Measure

Physician performance on prediction of PPCS was measured and compared with PPCS risk score performance. A risk assessment tool should outperform clinician accuracy to be relevant.[24] Treating physicians completed standardized surveys, which included the following question: "How likely is this patient to develop persistent symptoms beyond 1 month?" (response options: 0%-10%, 11%-20%, 21%-30%, 31%-50%, 51%-70%, 71%-90%, and 91%-100%).

Statistical Analysis

Forty-six variables were selected a priori for assessment based on a national planning meeting, recent systematic reviews, previous studies, and clinical experience.[16] Factors occurring after the ED assessment (eg, compliance with recommendations regarding rest or exertion) were omitted because this would reduce the face validity of a predictive score. At a subsequent consensus meeting, the total parent-reported Postconcussion Symptom Inventory score obtained during the ED visit was separated into its 20 individual com-

ponents and each was analyzed as independent candidate variable scores.

Based on the pilot study, it was estimated that 25% of participants would experience PPCS when applying *ICD-10* criteria.[9] Including 10 events per each candidate predictor variable,[17] 345 cases of PPCS would be required after screening for acceptable interrater agreement, assuming a dropout rate of 25% for the a priori selected variables.[27] To obtain 345 cases of PPCS, 1380 patients with new concussion had to be enrolled. Factoring a loss to follow-up rate of 23% based on pilot data,[28] the final derivation cohort sample size required was 1792 patients. To capture potential seasonal variability in PPCS rates, a 1-year enrollment period was required.

Based on a survey of PERC members,[29] 90% sensitivity was targeted to predict PPCS. To validate PPCS risk score with clinically acceptable confidence bounds (95% CI, 85%-95%), 200 patients with PPCS were required in a separate validation cohort. Assuming a rate of PPCS of 25%, 800 patients with new concussion had to be enrolled. With a loss to follow-up rate of 15% based on the derivation phase, the required validation sample size was 920 patients.

Descriptive statistics were used to summarize baseline characteristics. The differences between children with and without PPCS were assessed using the χ^2 test or the Fisher exact test as appropriate. Emphasizing clinical relevance and face validity, predictors with continuous outcomes were categorized or dichotomized. Interrater agreement was assessed for all candidate variables using the κ statistic; those variables with acceptable reliability (κ ≥0.6) remained eligible for the multivariable analysis.[24] Missing data were handled via list-wise deletion.

All reliable variables associated with PPCS ($P < .20$) were entered into a multivariable model using forward stepwise binary logistic regression analysis ($P = .05$ included but $P = .10$ removed). Variables in the regression model were assessed for co-linearity using the variance inflation factor.

The risk score was evaluated as a diagnostic test calculating sensitivity, specificity, and positive and negative likelihood ratios. The final model was validated internally using bootstrap resampling.[30] A risk score for the final multivariable model was derived using the model by Sullivan et al,[31] in which points were assigned to each predictor variable with point totals corresponding to risk estimate. High- and low-risk cut points for the PPCS risk score were determined by consensus at a team meeting following the derivation phase.

Temporal validation was performed using a separate independent cohort in the same institutions from which the derivation data were collected (ie, no data from the validation cohort were used to derive the risk score, and no data from the derivation cohort were used to validate). Validation performance was evaluated with correlated receiver operating characteristic analysis and test characteristics. Score calibration was assessed using the Hosmer-Lemeshow test and graphically using a calibration plot.[32]

Physicians' prediction was analyzed by logistic regression to predict PPCS. The accuracy of the validated risk stratification score was compared with that of physicians' predictions using the receiver operating characteristic analysis by DeLong et al.[33]

Statistical analyses were performed using SPSS Statistics versions 21 and 23 (SPSS Inc) and R version 3.0.2 (R Foundation for Statistical Computing). Two-sided *P* values of less than .05 were considered statistically significant.

Results

Patient Characteristics

There was complete assessment of the primary outcome of PPCS for 1701 of 2006 participants (84.8%) in the derivation cohort and 883 of 1057 participants (83.5%) in the validation cohort (Figure 1). The median age for both cohorts was 12.0 years (interquartile range, 9.2-14.6 years). The baseline patient characteristics appear in **Table 1**. Details about the injuries sustained and the types of medications used appear in **Table 2**.

The characteristics of patients with missing primary outcome data appear in eTable 2 in Supplement 2. The type of treatments provided in the ED appear in eTable 3.

Derivation Cohort

Bivariable Analysis

There were 510 participants (30.0%) who met the criteria of having PPCS in the derivation cohort. Forty-seven potential predictor variables were associated with PPCS in the bivariable analysis (**Table 3**, **Table 4**, and eTable 4 in Supplement 2). There were 294 patients (15%) who had blinded duplicate assessments (research assistant only: n = 145 [7%]; physician only: n = 92 [5%]; both research assistant and physician: n = 57 [3%]). Excellent overall interrater agreement was demonstrated (median κ = 0.97 [κ interquartile range, 0.75-0.99]).

Multivariable Analysis

The final multivariable model included (1) age, (2) sex, (3) prior concussion with symptom duration of longer than 1 week, (4) physician-diagnosed migraine history, (5) headache, (6) sensitivity to noise, (7) fatigue, (8) answering questions slowly, and (9) abnormal tandem stance (**Table 5**). The area under the curve (AUC) was 0.71 (95% CI, 0.69 to 0.74; eFigure 2 in Supplement 2). All variables had a variance inflation factor of less than 2.5, indicating a lack of multicollinearity between predictors.

Bootstrapping analysis (ie, resampling the model 1000 times) revealed a mean overoptimism value of 0.01 (95% CI, -0.02 to 0.03) and a corrected AUC of 0.70. In the final derivation model, 94.3% (1604/1701) of the participants with primary outcome data had complete data on all 9 predictor variables included in the multivariable model. The PPCS risk score derived from the multivariable model (score range, 0 to 12) linearly corresponded to risk estimate. Three cutoff points were selected to stratify PPCS risk (low risk: ≤3 points; medium risk: 4-8 points; and high risk: ≥9 points; **Table 6**).

Validation Cohort

There were 291 patients (33.0%) who met the criteria of having PPCS. The AUC for the model was 0.68 (95% CI, 0.65-0.72). For low-risk patients (≤3 points), the sensitivity was

Table 1. Baseline Patient Characteristics[a]

	Derivation Cohort (n = 2006)	Validation Cohort (n = 1057)	*P* Value
Age group, y			
5-7	377 (18.8)	157 (14.9)	
8-12	845 (42.1)	437 (41.3)	.01
13-<18	784 (39.1)	464 (43.9)	
Age, median (IQR), y	11.8 (8.9-14.6)	12.3 (9.6-14.8)	
Female sex	765 (38.1)	440 (41.6)	.06
Time between ED visit and head injury, median (IQR), h	2.8 (1.4-11.1)	3.0 (1.5-12.6)	.16
No. of prior concussions			
0	1532 (76.4)	816 (77.2)	
1	292 (14.6)	159 (15.0)	
2	105 (5.2)	45 (4.3)	
3	43 (2.1)	16 (1.5)	.38
4	13 (0.6)	6 (0.6)	
5	4 (0.2)	0	
≥6	5 (0.2)	6 (0.6)	
Longest symptom duration of prior concussion, wk			
<1	201 (10.0)	98 (9.3)	
1-2	101 (5.0)	55 (5.2)	
3-4	69 (3.4)	27 (2.6)	.47
5-8	31 (1.5)	18 (1.7)	
>8	55 (2.7)	34 (3.2)	
Prior treatment for headache	353 (17.6)	165 (15.6)	.19
Migraine			
Physician-diagnosed history	242 (12.1)	150 (14.2)	.09
Family history	931 (46.4)	505 (47.8)	.34
Developmental disorders			
Learning disabilities	179 (8.9)	64 (6.1)	.01
Attention-deficit disorder or attention-deficit/hyperactivity disorder	190 (9.5)	78 (7.4)	.06
Other	70 (3.5)	52 (4.9)	.05
Psychiatric disorders			
Anxiety	153 (7.6)	84 (7.9)	.72
Depression	45 (2.2)	42 (4.0)	.01
Sleep disorder	41 (2.0)	21 (2.0)	>.99
Other	12 (0.6)	20 (1.9)	.001
Loss of consciousness	239 (11.9)	156 (14.8)	.05
Duration of loss of consciousness, median (IQR), min	0.5 (0.2-1.0)	0.3 (0.1-1.0)	.98
Seizure	38 (1.9)	19 (1.8)	>.99
Appears dazed and confused	971 (48.4)	533 (50.4)	.31
Appears confused about events	486 (24.2)	269 (25.4)	.45
Answering questions slowly	806 (40.2)	447 (42.3)	.26
Repeats questions	270 (13.5)	148 (14.0)	.70
Forgetful of recent information	411 (20.5)	232 (21.9)	.35
No early signs of confusion or forgetfulness	726 (36.2)	354 (33.5)	.14

Abbreviations: ED, emergency department; IQR, interquartile range.

[a] Data are expressed as No. (%) unless otherwise indicated.

93.5% (95% CI, 90.0%-95.8%), specificity was 18.1% (95% CI, 15.2%-21.4%), and the negative likelihood ratio was 0.36 (95% CI, 0.23-0.58); the negative predictive value was 84.9% (95% CI, 77.6%-90.1%) and the positive predictive value was 35.9% (95% CI, 32.6%-39.5%).

For high-risk patients (≥9 points), the specificity was 93.4% (95% CI, 91.1%-95.1%), sensitivity was 20.3% (95% CI, 16.1%-25.3%), and the positive likelihood ratio was 3.00 (95% CI, 2.06-4.37); the negative predictive value was 70.4% (95% CI, 67.1%-73.5%) and the positive predictive value was 59.6% (95% CI, 50.3%-69.3%).

Validation test characteristics for all point values appear in eTable 5 in Supplement 2. The posttest probabilities for the 3 risk strata (low, medium, and high) appear in eTable 6. The Hosmer-Lemeshow test indicated goodness of fit for the model (*P* = .50). The calibration plot of observed frequency com-

Table 2. Mechanism and Types of Injuries Sustained and Medications Used to Treat Patients

	No. (%) of Patients		
	Derivation Cohort (n = 2006)	Validation Cohort (n = 1057)	*P* Value
Mechanism of injury			
Sports or recreational play	1349 (67.2)	722 (68.3)	.56
Non-sports-related injury or fall	495 (24.7)	246 (23.3)	
Motor vehicle collision	36 (1.8)	19 (1.8)	
Assault	22 (1.1)	17 (1.6)	
Other	98 (4.9)	46 (4.4)	
Playing sports or recreational play while injured			
Hockey	302 (15.1)	157 (14.9)	<.001
Football	87 (4.3)	30 (2.8)	
Soccer	171 (8.5)	102 (9.6)	
Skiing or snowboarding	63 (3.1)	53 (5.0)	
Skating	20 (1.0)	13 (1.2)	
Baseball or softball	20 (1.0)	5 (0.5)	
Bicycling	49 (2.4)	5 (0.5)	
Horseback riding	13 (0.6)	6 (0.6)	
Skateboarding or rollerblading	15 (0.7)	6 (0.6)	
Basketball	79 (3.9)	50 (4.7)	
Trampoline	15 (0.7)	4 (0.4)	
Gymnastics	12 (0.6)	13 (1.2)	
Tobogganing	30 (1.5)	13 (1.2)	
Recreational play (gym or recess)	252 (12.6)	110 (10.4)	
Other	219 (10.9)	154 (14.6)	
Use of protective gear			
Helmet	522 (26.0)	257 (24.3)	
Mouth guard	302 (15.1)	146 (13.8)	
Type of non-sports-related injury or fall			
Slipped, fell, or tripped on the ground	211 (10.5)	119 (11.3)	.69
Struck head against wall or door	71 (3.5)	31 (2.9)	
Fell from height	74 (3.7)	31 (2.9)	
Struck head against household object	60 (3.0)	26 (2.5)	
Fell down stairs	23 (1.1)	14 (1.3)	
Struck by object	53 (2.6)	24 (2.3)	
Injury involved a fall	1029 (51.3)	581 (55.0)	.03
Motor vehicle-related collision			
Passenger in car	23 (1.1)	12 (1.1)	.70
Driver of car	4 (0.2)	5 (0.5)	
Pedestrian	7 (0.3)	1 (0.1)	
Cyclist	1 (0.1)	0	
Other	1 (0.1)	1 (0.1)	
Use of medications			
Received during time of injury	1070 (53.3)	602 (57.0)	.03
Acetaminophen	491 (24.5)	287 (27.2)	.12
Ibuprofen	663 (33.1)	367 (34.7)	.34
Dimenhydrinate	24 (1.2)	12 (1.1)	>.99
Other	87 (4.3)	56 (5.3)	.21

pared with the predicted probability of PPCS showed an intercept of 0.07 and a slope of 0.90, suggesting acceptable calibration (eFigure 3).

The data for physicians' prediction at time of emergency department visit for probability of PPCS at 28 days appear in **Table 7**. A model with 9 variables from the risk score as well as physicians' prediction had an AUC of 0.68 (95% CI, 0.63-0.73), whereas physicians' prediction alone had an AUC of 0.55 (95% CI, 0.50-0.59; **Figure 2**). Thus, in the validation cohort, the addition of the derived prediction model to the physicians' judgment alone resulted in an incremental C statistic improvement of 0.13 (95% CI, 0.07-0.20; $P < .001$).

Table 3. Demographic and Medical History Variables of Patients With Persistent Postconcussive Symptoms (PPCS) at 28 Days in the Derivation Cohort

	No. With PPCS/ Total No. ofPatients (%)	*P* Value[a]	Odds Ratio (95% CI)	AUC	κ[b]
Age group, y					
5-7	57/318 (17.9)	<.001	1 [Reference]	0.61	1.00
8-12	191/726 (26.3)		1.6 (1.2-2.3)		
13-<18	262/657 (39.9)		3.0 (2.2-4.2)		
Sex					
Male	244/1054 (23.1)	<.001	1 [Reference]	0.60	0.95
Female	266/647 (41.1)		2.3 (1.9-2.9)		
No. of prior concussions					
0	371/1307 (28.4)	.01	1 [Reference]	0.53	0.98
≥1	136/388 (35.1)		1.4 (1.1-1.7)		
Prior concussion and symptom duration					
No prior concussion; symptom duration <1 wk	165/406 (40.6)	<.001	1 [Reference]	0.55	1.00
Prior concussion; symptom duration ≥1 wk	101/219 (46.1)		2.2 (1.7-3.0)		
Time from last concussion					
<1 mo	12/35 (34.3)	.58	1 [Reference]	0.53	0.68
1 mo to <1 y	48/124 (38.7)		1.2 (0.6-2.7)		
≥1 y	74/223 (33.2)		1.0 (0.4-2.0)		
Physician-diagnosed migraine history					
No	419/1489 (28.1)	<.001	1 [Reference]	0.54	0.90
Yes	87/204 (42.6)		1.9 (1.4-2.6)		
Learning disabilities					
No	452/1550 (29.2)	.03	1 [Reference]	0.52	0.87
Yes	55/145 (37.9)		1.5 (1.0-2.1)		
Attention-deficit disorder or attention-deficit/ hyperactivity disorder					
No	456/1543 (29.6)	.23	1 [Reference]	0.51	0.96
Yes	51/149 (34.2)		1.2 (0.9-1.8)		
Anxiety					
No	459/1568 (29.3)	.05	1 [Reference]	0.51	1.00
Yes	49/131 (37.4)		1.4 (1.0-2.1)		
Depression					
No	490/1663 (29.5)	.002	1 [Reference]	0.51	1.00
Yes	19/36 (52.8)		2.7 (1.4-5.2)		
Loss of consciousness					
No	374/1292 (28.9)	.04	1 [Reference]	0.52	1.00
Yes	72/199 (36.2)		1.4 (1.0-1.9)		
Appears dazed and confused					
No	233/873 (26.7)	<.001	1 [Reference]	0.54	0.59
Yes	277/828 (33.5)		1.2 (0.5-3.2)		
Appears confused about events					
No	370/1292 (28.6)	.03	1 [Reference]	0.52	0.70
Yes	140/409 (34.2)		1.2 (0.5-3.2)		
Answering questions slowly					
No	262/1024 (25.6)	<.001	1 [Reference]	0.56	0.68
Yes	248/677 (36.6)		1.2 (0.5-3.2)		

Abbreviation: AUC, area under the curve.

[a] Calculated using the χ^2 test or the Fisher exact test. All variables from this Table and in Table 4 with *P* < .20 were entered into the full model analysis.

[b] There were 294 patients (15%) who had blinded duplicate assessments (research assistant only: n = 145; physician only: n = 92; both research assistant and physician: n = 57).

Discussion

A PPCS clinical risk score derived in a large, diverse cohort of children presenting to the ED with concussion within 48 hours of head injury was significantly better than physician judgment in predicting future PPCS, although the discrimination of the risk score model was modest (AUC of 0.71). The PPCS risk score incorporates 9 clinical variables containing information from demographics, history, initial symptoms, cognitive complaints, and physical examination. Evaluation in an independent validation cohort demonstrated good test characteristic retention.

Table 4. Medical History, Injury, and Assessment Score Variables of Patients With Persistent Postconcussive Symptoms (PPCS) at 28 Days in the Derivation Cohort

	No. With PPCS/ Total No. of Patients (%)	*P* Value[a]	Odds Ratio (95% CI)	AUC	κ[b]
Repeats questions					
No	427/1477 (28.9)	.01	1 [Reference]	0.52	0.71
Yes	83/224 (37.1)		1.2 (0.5-3.2)		
Forgetful of recent information					
No	381/1353 (28.2)	.001	1 [Reference]	0.54	0.68
Yes	129/348 (37.1)		1.5 (1.2-1.9)		
Positive change in headache score					
No	35/226 (15.5)	<.001	1 [Reference]	0.55	1.00
Yes	451/1414 (31.9)		2.6 (1.8-3.7)		
Positive change in sensitivity to noise score					
No	259/1082 (23.9)	<.001	1 [Reference]	0.59	0.97
Yes	227/558 (40.7)		2.2 (1.8-2.7)		
Positive change in fatigue score					
No	82/432 (19.0)	<.001	1 [Reference]	0.57	0.97
Yes	404/1207 (33.5)		2.1 (1.6-2.8)		
Mechanism of injury					
Sports or recreational play	350/1154 (30.3)	.23	1 [Reference]	0.52	0.92
Non-sports-related injury or fall	116/412 (28.2)		0.9 (0.7-1.2)		
Motor vehicle collision	16/34 (47.1)		2.0 (1.0-4.1)		
Assault	5/19 (26.3)		0.8 (0.3-2.2)		
Other	23/81 (28.4)		0.9 (0.6-1.5)		
Standardized Assessment of Concussion tool (form C) total score[c]					
≤0.11	285/915 (31.1)	.25	1 [Reference]	0.50	0.98
>0.11	220/770 (28.6)		0.9 (0.9-1.1)		
Balance Error Scoring System tandem stance No. of errors[d]					
0-3	272/990 (27.5)	.007	1 [Reference]	0.54	0.76
≥4 or Physically unable to undergo testing	232/427 (54.3)		1.3 (1.0-1.7)		
Glasgow Coma Scale score[e]					
14	7/19 (36.8)	.50	1 [Reference]	0.50	0.94
15	456/1534 (29.7)		0.7 (0.3-1.8)		
Normal neck range of motion					
No	29/76 (38.2)	.10	1 [Reference]	0.51	0.29
Yes	427/1461 (29.2)		1.5 (0.9-2.4)		
Neck tenderness					
No	76/335 (22.7)	.01	1 [Reference]	0.53	0.44
Yes	122/1461 (8.4)		1.4 (1.1-1.8)		

Abbreviation: AUC, area under the curve.

[a] Calculated using the χ^2 test or the Fisher exact test. All variables in this Table and in Table 3 with $P < .20$ were entered into the full model analysis.

[b] There were 294 patients (15%) who had blinded duplicate assessments (research assistant only: n = 145; physician only: n = 92; both research assistant and physician: n = 57).

[c] Measures and assigns points for orientation (maximum: 4 points), immediate memory (maximum: 15 points), concentration (maximum: 6 points), and recall (maximum: 5 points). The total points (maximum: 30 points) were calculated. A higher score indicates better cognitive function. Because performance is correlated with age, the total score in the analysis was standardized (mean [SD], 0 [1]) for age using norms.

[d] Assesses static postural stability. In tandem stance, the participant is instructed to stand heel to toe with the nondominant foot in the back and to hold this stance for 20 seconds with hands on hips and eyes closed. The modified version of this test is calculated by adding 1 error point for each error during the 20-second test; total scores range from 0 to 10. A higher score indicates poorer postural stability.

[e] A neurological scale that measures state of consciousness. Scores are assigned for eye opening (4 points), verbal response (5 points), and motor (6 points); total scores range from 3 to 15. A higher score indicates greater alertness.

Even though prior research found an association between prolonged recovery and total postinjury symptom burden score (22 items using a 7-point scale),[34] such a complex scale is a barrier to adoption by acute care clinicians.[24] We instead analyzed individual symptoms, resulting in a final model that includes 4 early symptoms and signs in the PPCS risk score. Several final model variables have been associated with PPCS, including headache, answering questions slowly, and sensitivity to noise.[9,11,35] Female sex and older age are associated with prolonged recovery in children and adults.[9,35]

Although the clinical utility of the PPCS risk score will need to be assessed in an externally validated implementation study

Table 5. Selected Predictor Variables for Multivariable Model of Persistent Postconcussive Symptoms (PPCS) at 28 Days in the Derivation Cohort[a]

	No. of Risk Points for PPCS	Odds Ratio (95%CI)	*P* Value
Age group, y			
5-7	0	1 [Reference]	<.001
8-12	1	1.54 (1.09-2.19)	
13-<18	2	2.31 (1.62-3.32)	
Sex			
Male	0	1 [Reference]	<.001
Female	2	2.24 (1.78-2.82)	
Prior concussion and symptom duration			
No prior concussion; symptom duration <1 wk	0	1 [Reference]	.01
Prior concussion; symptom duration ≥1 wk	1	1.53 (1.10-2.13)	
Physician-diagnosed migraine history			
No	0	1 [Reference]	.001
Yes	1	1.73 (1.24-2.43)	
Answering questions slowly			
No	0	1 [Reference]	.008
Yes	1	1.37 (1.08-1.74)	
Balance Error Scoring System tandem stance No. of errors			
0-3	0	1 [Reference]	.02
≥4 or Physically unable to undergo testing	1	1.31 (1.04-1.66)	
Headache			
No	0	1 [Reference]	.01
Yes	1	1.66 (1.11-2.48)	
Sensitivity to noise			
No	0	1 [Reference]	.002
Yes	1	1.47 (1.15-1.87)	
Fatigue			
No	0	1 [Reference]	<.001
Yes	2	1.84 (1.37-2.46)	

[a] There were 1701 patients in the derivation cohort included in the primary analysis.

Table 6. Risk Categories for Persistent Postconcussive Symptoms (PPCS) in the Derivation Cohort[a]

PPCS Risk Category	Total No. of Risk Points	Estimated Risk of PPCS, % (95% CI)	No. With PPCS/ Total No. of Patients (%)
Low risk	0	4.1 (2.4-6.7)	0/6 (0)
	1	5.8 (3.9-9.5)	6/37 (16.2)
	2	8.3 (6.0-13.2)	11/98 (11.2)
	3	11.8 (8.5-17.8)	15/165 (9.1)
Medium risk	4	16.4 (11.9-22.4)	41/239 (17.2)
	5	22.3 (16.7-29.7)	71/289 (24.6)
	6	29.7 (22.7-37.9)	90/299 (30.1)
	7	38.2 (30.1-46.9)	96/243 (39.5)
	8	47.6 (38.9-57.1)	80/172 (46.5)
High risk	9	57.1 (48.2-65.6)	58/103 (56.3)
	10	66.1 (57.2-74.4)	30/43 (69.8)
	11	74.1 (65.8-81.5)	9/13 (69.2)
	12	80.8 (74.6-88.3)	3/3 (100)

[a] There were 1701 patients in the derivation cohort included in the primary analysis.

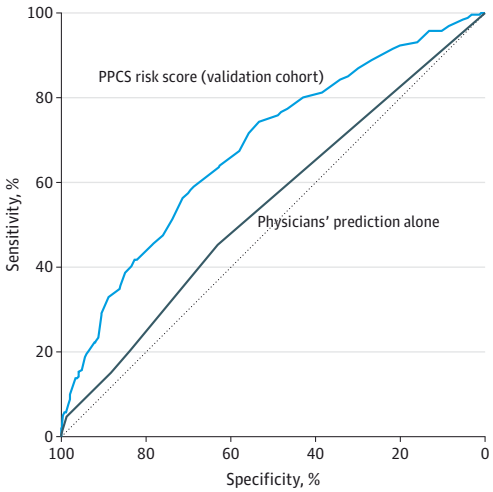
prior to adoption into routine practice, the risk stratification score has the potential to individualize concussion care through optimal symptom management and appropriate follow-up.[9,16] Therefore, future research needs to determine if the moderate test characteristics of the PPCS risk score allow for clinicians to confidently provide reassurance, alter management plans, or both. Future clinical benefits might include identifying high-risk individuals for further screening, prioritization for specialized concussion evaluations, and initiation of emerging treatments to prevent PPCS.[36]

Table 7. Physicians' Prediction at Time of Emergency Department Visit for Probability of Persistent Postconcussive Symptoms (PPCS) at 28 Days in the Derivation Cohort

Physicians' Prediction for Probability of Developing PPCS, %	No. With PPCS/ Total No. of Patients (%)
0-10	194/718 (27.0)
11-20	96/282 (34.0)
21-30	48/117 (41.0)
31-50	21/59 (35.6)
51-70	12/24 (50.0)
71-90	6/11 (54.5)
91-100	3/5 (60.0)
Total[a]	380/1216 (31.3)

[a] Physicians' predictions at the time of the emergency department visit for patients who completed follow-up at 28 days.

Figure 2. Receiver Operating Characteristic Curves



PPCS indicates persistent postconcussive symptoms. The area under the curve was 0.71 (95% CI, 0.69-0.74) for the derivation cohort and 0.68 (95% CI, 0.65-0.72) for the validation cohort.

Strengths of this study include standardized assessment of predictor and outcome variables using validated scales in a cohort with acute concussions (exclusion of presentations >48 hours after injury). Moreover, a large, cross-country, multisite validation cohort confirmed good predictive performance of the risk score model used in the derivation cohort. Inclusion of participants from a wide age range and spectrum of injuries and those with behavioral, learning, and psychological problems enhances generalizability.

There were minor baseline differences between the derivation and validation cohorts (eg, age group, learning disabilities, depression, and type of sports played). These differences increase the generalizability of our model. Therefore, we believe our findings are applicable to the assessment of children seeking acute care following a concussive event.

Despite collective agreement across guidelines that initial management should include physical and cognitive rest followed by graduated return to normal activities, wide practice variation exists.[29,37] The lack of evidence for initial management of concussion (including protocols regarding timing of returning to activity) is a crucial issue in the field of pediatric concussion, and results of this study should be applied in urgently needed future comparative clinical trials.[38] The PPCS risk score will benefit concussion care research by providing a tool for the targeted selection of patients in greatest need of intervention.[9] Selection of pediatric patients at high risk for PPCS may optimize research recruitment by offering more efficient and cost-effective enrollment strategies, or may be used to stratify participants in clinical trials according to PPCS risk.

Because no objective criterion standards for concussion or PPCS diagnoses exist (ie, no readily available biomarkers or imaging modalities),[39] the PPCS risk prediction score may be less precise than prediction studies for other diseases. Nonetheless, the outcome measures used in this study generated the best-available evidence through the use of validated tools. In addition, the definitions we used aligned with current concussion guidelines and *ICD-10* standards.[18,26,40] The PPCS risk model demonstrated only modest ability to discriminate patients who will and will not have PPCS, resulting in erroneous categorization. Test characteristics could be further refined through inclusion of biomarkers, genetic data, or advanced neuroimaging techniques. The pragmatic, generalizable PPCS risk model does not require expensive and painful testing, and could therefore be used to triage initial management.

There are several limitations to this study. Selection bias may limit generalizability. The patients with concussion in our derivation and validation cohorts may have higher PPCS rates and different risk characteristics than those patients with less severe injuries who may have not sought pediatric ED care. Nonetheless, the study included a heterogeneous population recruited through the use of a large number of study sites with great geographical variation.

Even with inclusion of concussions sustained by a variety of mechanisms, some of which may have involved higher forces than those generally seen in sports (eg, motor vehicle collisions), we observed similar rates of PPCS and loss of consciousness as the rates in the sideline assessment and outpatient literature.[41-43] Because it is possible that the PPCS risk score may not perform as well in different populations, validation should occur in other clinical settings, such as nontertiary care EDs, primary care, and sideline assessments.

In addition, the sample was limited to participants without observable lesions on imaging; therefore, it may not be representative of a more complicated spectrum of mild traumatic brain injury. However, because the presence of an intracranial lesion on standard imaging no longer meets the current concussion definition,[18,40] outcome prediction in this population is beyond the study's scope. Future research should seek to determine the performance of this PPCS risk assessment tool in a nuanced population of patients with mild traumatic brain injury.

Although other injuries might have contributed to ongoing symptoms, patients with multisystem injuries requiring hospitalization were excluded. An additional limitation is that measures of socioeconomic status or family functioning were

not included, which are variables that could have an effect on follow-up care and resources thus affecting symptom burden with alteration of PPCS risk.

Even though the study had missing data, it was limited in scope. Baseline characteristics were similar between those with and without the primary outcome in both the derivation and validation cohorts, and most enrolled participants had no missing data.

Given the wide age range, potential variation exists in respondent type (parent vs patient); however the Postconcussion Symptom Inventory has good parent and self-report correlation.[22] In addition, without a control group, we cannot definitively attribute ongoing symptoms to the acute injury. However, literature examining PPCS incidence in patients with head injury compared with controls (eg, orthopedic injury) has yielded similar rates in the head injury group as in our cohort.[9]

Conclusions

A clinical risk score developed among children presenting to the ED with concussion and head injury within the previous 48 hours had modest discrimination to stratify PPCS risk at 28 days. Before this score is adopted in clinical practice, further research is needed for external validation, assessment of accuracy in an office setting, and determination of clinical utility.

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