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DEVELOPMENT AND VALIDATION OF A PREDICTIVE MODEL FOR CHILDHOOD MORTALITY AFTER A TRAUMATIC BRAIN INJURY: ANALYSIS OF THE NATIONAL TRAUMA DATA BANK

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Introduction

TBI is a significant cause of mortality in the pediatric age group. Patients who receive early, evidence-based interventions show improved recovery process and reduced mortality rate. However, treatment methods tend to vary with patient-level factors. Recent advances in prognostic modeling demonstrate promising capabilities in predicting survival probabilities and patient outcomes from complex, multidimensional clinical data. They are able to process real-time data (i.e., patient demographics, injury characteristics, and clinical parameters) that are routinely available at hospital admission, and thus, have the potential to provide timely accurate prognoses. Thus, creating a dynamic, patient-specific prognostic model would assist clinicians with timely medical decisions, triage patients effectively, and potentially mitigate poor outcomes.

Objectives

- Develop and validate a clinical tool for predicting mortality in children (aged ≤ 18 years) with mild to severe TBI.
- Translate our findings into a web-based tool that can be used in clinical practice to calculate and predict the risk of mortality among TBI patients at the time of hospital admission.

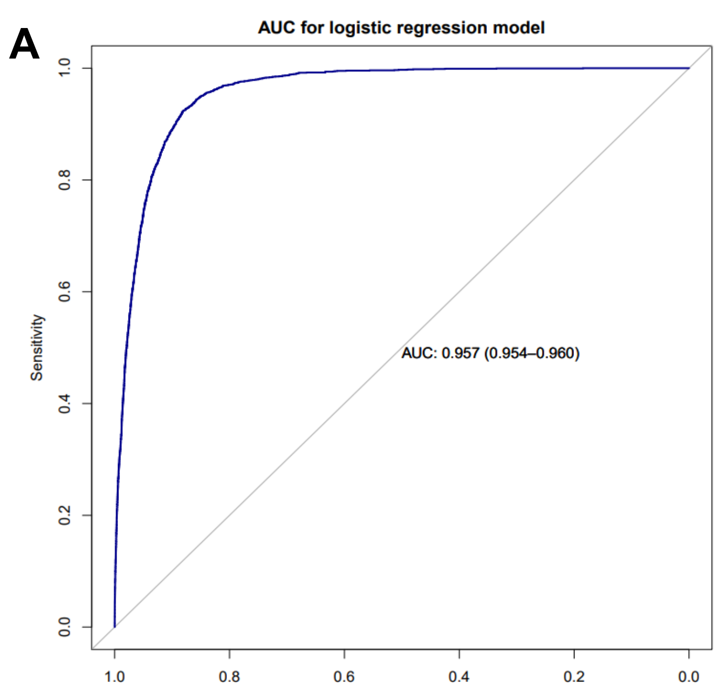
Materials and Methods

- This is a predictive study of patient data derived from the National Trauma Data Bank (NTDB) from 2007 to 2015.
- This study adhered to the guidelines set by the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis.
- We selected all children (≤18 years) who incurred a traumatic brain injury (TBI), defined according to ICD9 code in the NTDB. We excluded patients with unreported age and those that died on transport or once admitted to the emergency department (ED).
- The primary outcome was in-hospital death. The clinical variables of interest included patient age, gender, race, ethnicity, vitals in the ED, and intent. We also incorporated mode of transportation, time to hospital arrival from 911 call, ED vitals, and ED Glasgow coma scale (GCS), injury type, and mechanism.
- We tabulated descriptive statistics of all patients, and separated by survivors and non-survivors. Continuous variables were presented as median with interquartile range (IQR) and analyzed by Wilcoxon rank-sum test. Categorical data were reported as number with percent and analyzed by the Chi-square test.
- A p-value <5% denoted statistical significance. All analyses were performed with R version 4.0.2.
- We used predictive mean matching and simple bootstrapping methods to impute numeric, categorical, and continuous variables.
- Samples were randomly split into a training set (70%) and a test set (30%).
- In the test set, we measured the prediction performance by computing the C-statistic (e.g., area under the receiver operating characteristic [ROC] curve), accuracy, sensitivity, specificity, and precision. Furthermore, we conducted a decision curve analysis to assess the net benefit of our prediction models over prediction probability of the reference model. Dynamic nomogram was created in Rshiny

Results

- A total of 124,078 children were included in the study (69% male; median [IQR] age, 13.0 [6.0, 16.0.] years; 69% White), 5.5% (n=6,862) of whom died.
- Those who died were older (16 vs. 12 years, p<5%), arrived faster to the ER (69 vs. 52 minutes, p<5%), had a lower GCS (15 vs. 3, p<5%), and higher ISS (30 vs. 14, p<5%) compared to the survivors.
- Unintentional injuries were the most common among both the survivors and non-survivors (94% vs. 80%, respectively, p<5%).
- The final model had 13 variables that performed well with a high discriminative performance (C-statistic of 95.7%; 95% CI, 95.4% - 96.0%) and accuracy of 95.2%.
- The prognostic model reached a precise calibration curve suggesting a strong agreement between the predicted and observed number of events
- A dynamic nomogram of the validated logistic model was developed as a translational tool for healthcare providers to use in clinical settings.

A



B

Model	C-statistic	Accuracy	Sensitivity	Specificity	Precision
Logistic regression	95.7 % (95.4-96.0)	95.2%	65.3%	96.1%	32.8%

Figure 1. Prediction ability of the logistic regression model.
(A) Receiver operating characteristic curve showing a high discriminative ability with an AUC of 0.957 (95% CI = 0.954 – 0.960).
(B) The prognostic model achieved a high accuracy (95.2%) and specificity (96.1%).

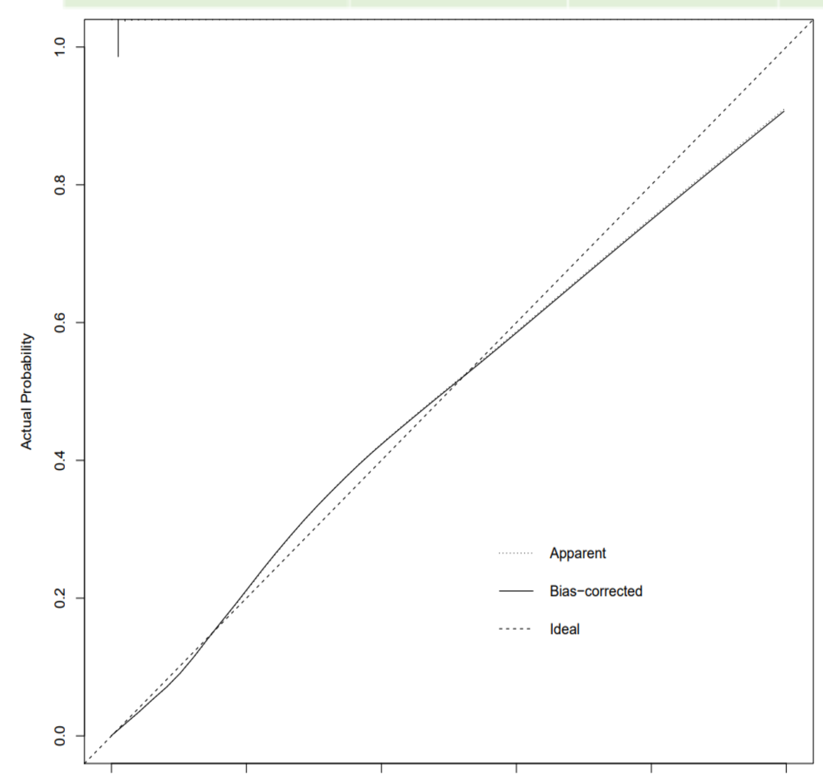


Figure 2. Calibration plot for the TBI model based on admission characteristics.

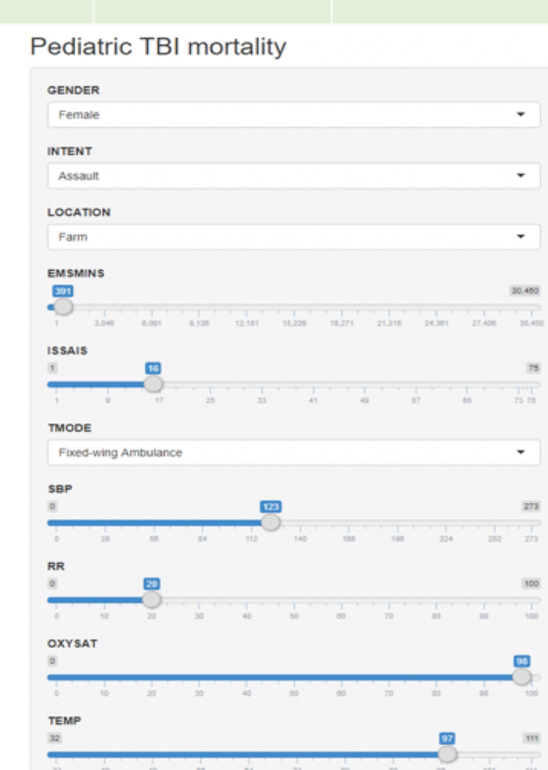


Figure 3. Online web-based calculator for predicting mortality among patients with TBI

Results

Table 1. Multivariable Regression Analysis of Characteristics of Children with TBI, 2007-2015, by survival status

Variable	Total (n=124,078)	Survived (n=117,216)	Died (n=6,862)	p value
Patient demographics				
Age	13.0 (6.0, 16.0)	12.0 (6.0, 16.0)	16.0 (9.0, 17.0)	<0.001
Sex				0.016
Female	39,061 (12%)	36,991 (32%)	2,070 (30%)	
Male	85,017 (69%)	80,225 (68%)	4,792 (70%)	
Race/Ethnicity				<0.001
Asian	2,534 (2%)	2,417 (2.1%)	117 (1.7%)	
Black	16,922 (14%)	15,398 (13%)	1,524 (22%)	
White	85,255 (69%)	81,095 (69%)	4,160 (61%)	
Other	19,367 (16%)	18,306 (16%)	1,061 (15%)	
Physiologic measures				
ISS	14 (9, 21)	14 (9, 19)	30 (25, 41)	<0.001
GCS	15 (10, 15)	15 (12, 15)	3 (3, 3)	<0.001
SBP (mm Hg)	122 (110, 135)	122 (110, 135)	114 (89, 140)	<0.001
Pulse (bpm)	99 (83, 116)	99 (83, 115)	107 (78, 134)	<0.001
Respiratory rate	20 (16, 24)	20 (16, 24)	16 (0, 20)	<0.001
Oxygen saturation (%)	100 (98, 100)	100 (98, 100)	99 (94, 100)	<0.001
Temperature (◦F)	97.88 (96.80, 98.60)	97.88 (96.98, 98.60)	96.80 (95, 97.88)	<0.001
RRAQ				<0.001
Assisted Respiratory Rate	20,154 (16%)	15,702 (13%)	4,452 (65%)	
Unassisted Respiratory Rate	103,924 (84%)	101,514 (87%)	2,410 (35%)	
Injury characteristics				
Intent				<0.001
Assault	6,753 (5.4%)	5,795 (4.9%)	958 (14%)	
Self-inflicted	639 (0.5%)	377 (0.3%)	262 (3.8%)	
Unintentional	115,858 (93%)	110,336 (94%)	5,522 (80%)	
Undetermined/Other	828 (0.7%)	708 (0.6%)	120 (1.7%)	
Location				<0.001
Farm	1,325 (1.1%)	1,276 (1.1%)	49 (0.7%)	
Home	32,935 (27%)	31,255 (27%)	1,680 (24%)	
Industry	352 (0.3%)	341 (0.3%)	11 (0.2%)	
Public Building	8,081 (6.5%)	7,929 (6.8%)	152 (2.2%)	
Recreation	16,821 (14%)	16,495 (14%)	326 (4.8%)	
Residential Institution	396 (0.3%)	384 (0.3%)	12 (0.2%)	
Street	57,740 (47%)	53,408 (46%)	4,332 (63%)	
Other	6,428 (5.2%)	6,128 (5.2%)	300 (4.4%)	
Transportation Mode				<0.001
Ground Ambulance	76,506 (62%)	72,756 (62%)	3,750 (55%)	
Helicopter	31,006 (25%)	28,161 (24%)	2,845 (41%)	
Police	558 (0.4%)	514 (0.4%)	44 (0.6%)	
Private/Public	13,678 (11%)	13,576 (12%)	102 (1.5%)	
Fixed-wing Ambulance	1,548 (1.2%)	1,460 (1.2%)	88 (1.3%)	
Other	782 (0.6%)	749 (0.6%)	33 (0.5%)	
EMS Minutes	68 (42, 183)	69 (42, 195)	52 (32, 92)	<0.001

GCS-Glasgow coma scale; ISS-injury severity score; SBP-systolic blood pressure; RRAQ-respiratory rate assessment qualifier; Continuous variables expressed as (median, IQR); Categorical variables expressed as n (%); Statistical test performed: Wilcoxon rank-sum test (continuous), Chi-square (categorical)

Conclusion

- Our results indicate several independent early factors significant in predicting mortality in children with mild to severe TBI
- We provide an accurate early prognostic model with high discriminative ability, accuracy, specificity, and calibration to measure the risk of mortality among children with mild to severe TBI.
- Our findings have led to a clinically translatable web-based tool to potentially provide a timely estimation of the risk of mortality among pediatric patients with TBI admitted to the ED.
- To our knowledge, this study is the largest study that uses a mathematical model to identify early predictors of mortality in children with mild to severe TBI and to develop a tool that can be easily used clinically.
- Future directions: externally validate the data and compare our model to other trauma scores used in children