TURKISH JOURNAL OF EMERGENCY MEDICINE

Original Article

Access this article online

Quick Response Code:

Website: www.turkjemergmed.com

DOI: 10.4103/2452-2473.336107

Development of a nomogram to predict the outcome of moderate or severe pediatric traumatic brain injury

Thakul Oearsakul, Thara Tunthanathip*

Department of Surgery, Division of Neurosurgery, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Abstract:

OBJECTIVES: Traumatic brain injury (TBI) in children has become the major cause of mortality and morbidity in Thailand that has had an impact with economic consequences. This study aimed to develop and internally validate a nomogram for a 6-month follow-up outcome prediction in moderate or severe pediatric TBI.

METHODS: This retrospective cohort study involved 104 children with moderate or severe TBI. Various clinical variables were reviewed. The functional outcome was assessed at the hospital discharge and at a 6-month follow-up based on the King's Outcome Scale for Childhood Head Injury classification. Predictors associated with the 6-month follow-up outcome were developed from the predictive model using multivariable binary logistic regression to estimate the performance and internal validation. A nomogram was developed and presented as a predictive model.

RESULTS: The mean age of the samples was 99.75 months (standard deviation 59.65). Road traffic accidents were the highest injury mechanism at 84.6%. The predictive model comprised Glasgow Coma Scale of 3–8 (odds ratio [OR]: 16.07; 95% confidence interval [CI]: 1.27–202.42), pupillary response in one eye (OR 7.74; 95% CI 1.26–47.29), pupillary nonresponse in both eyes (OR: 57.74; 95% CI: 2.28–145.81), hypotension (OR: 19.54; 95%: CI 3.23–117.96), and subarachnoid hemorrhage (OR: 9.01, 95% CI: 1.33–60.80). The concordance statistic index (C-index) of the model's discrimination was 0.931, while the C-index following the bootstrapping and 5-cross validation were 0.920 and 0.924, respectively.

CONCLUSIONS: The performance of a clinical nomogram for predicting 6-month follow-up outcomes in pediatric TBI patients was assessed at an excellent level. However, further external validation would be required for the confirmation of the tool's performance.

Keywords:

Brain injury, clinical prediction rules, nomogram, Traumatic brain injury

Submitted: 10-12-2020
Revised: 05-02-2021
Accepted: 07-02-2021
Published: 20-01-2022

ORCID:
TO: 0000-0003-3228-3431
TT: 0000-0002-6303-836X

Address for correspondence:
Dr. Thara Tunthanathip, Department of Surgery, Division of Neurosurgery, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: tsus4@hotmail.com

Introduction

Traumatic brain injury (TBI) is a serious public health problem, which in Thailand, TBI causes death, and incapacity in the population, particularly for children.[1] The mortality rate of TBI in children ranged 3.2%–5.2%, whereas severe disability was reported at 0.3%–0.8%.[2,3] Fulkerson *et al.* studied the outcome of TBI children who recorded a Glasgow Coma Scale (GCS) score of 3 or 4. They found that the mortality of children with a GCS of 3 and 4 was 61.4% and 43.5%, respectively, with a good recovery found in only 4.6%–8.7%. The predictors for survival included pupillary response, abuse mechanism, hypotension, hypothermia, and midline shift.[4]

Long-term sequelae of TBI patients would also be related to future productivity loss.[4,5]

How to cite this article: Oearsakul T, Tunthanathip T. Development of a nomogram to predict the outcome of moderate or severe pediatric traumatic brain injury. Turk J Emerg Med 2022;22:15-22.

Box-ED section

What is already known on the study topic?

Mortality and disability following traumatic brain injury (TBI) in children are major public health problems, particularly moderate or severe TBI

Prediction of the 6-month follow-up outcome in children following TBI is an essential strategy for resource allocation

A nomogram is one of the clinical prediction tools that has been well documented in the literature.

What does this study tell us?

This study presented the first analysis of a clinical nomogram to predict the 6-month follow-up in pediatric TBI patients with an excellent predictability

This could be used to provide external validation in future to apply a predictive model.

Nevertheless, in Thailand, preventive campaigns to reduce pediatric TBI have not dramatically decreased the number of road accidents involving children.[5] Thus, prediction of the functional outcome in pediatric patients following TBI is an important procedure for allocating resources and developing future health strategies. Hence, a nomogram is a clinical prediction tool that has been well documented in the literature.[6] Previous studies used a nomogram to predict both clinical outcomes and prognosis; such as neuro-oncology,[7] TBI,[8,9] stroke,[10] and posttraumatic seizure.[11] Tunthanathip and Udomwitthayaphiban studied TBI patients with penetrating injury and used a nomogram to predict the mortality. For the results, the nomogram had a sensitivity of 0.800, specificity of 0.926, positive predictive value of 0.727, negative predictive value of 0.950, and an area under the receiver operating characteristic curve (AUC) of 0.860.[8]

However, the predictive performance of a nomogram to determine the functional outcomes of pediatric TBI patients has never been assessed. To fill this knowledge gap, this present study developed and internally validated a nomogram for a 6-month follow-up outcome prediction in pediatric TBI.

Methods

Study design and setting

This historical cohort study reviewed the medical records of patients with TBI who were younger than 15 years and admitted at a trauma center located in Southern Thailand between January 2009 and January 2020.

Study population

All TBI patients who had a postresuscitation GCS of 3–12 were included in the study. Exclusion criteria were patients who had died before arrival, died within the first 24 h following TBI, and those who did not undergo a computed tomography (CT) scan of the brain.

Sample size estimation

The authors used the formula in the "statistics and sample size pro" application for calculating the sample size for the diagnostic tests.[12] By providing the input from the previous study[10] (prevalence: 32.3; sensitivity: 0.8), the sample size should include at least 62 patients.

Methods and measurements

The demographics, neuroimaging, and treatment on admission were reviewed for analysis. Because hypotension causes a misinterpetation of the GCS score from poor cerebral perfusion, the GCS score collected in the present study was the patient's GCS score with the stable vital signs following resuscitation at the emergency department.[3] Moreover, the GCS score after resuscitation was categorized into moderate TBI (GCS score of 9–12) and severe TBI (GCS score of 3–8),[11] while hypotension and bradycardia were defined based on the age of the patient.[8] The findings from the CT of the brain, type of intracranial injuries, midline shift, and obliteration of the basal cistern were reviewed by two neurosurgeons. Based on Vieira *et al*., diffuse axonal injury (DAI) was defined where patients had signs of DAI from a CT scan or magnetic resonance imaging.[13]

Outcomes

According to the King's Outcome Scale for Childhood Head Injury (KOSCHI) classification, the functional outcome of this study was assessed at the hospital discharge and at a 6-month follow-up visit.[4] The authors evaluated the outcomes by telephone for patients who did not attend the follow-up. The study was approved by the Human Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC.63-373-10-1, Date: 29.09.2020).

Statistical analysis

The demographic data, neuroimaging findings, treatment, and the KOSCHI classification were calculated from descriptive statistics. These were reported as percentages for the categorical data and mean ± standard deviation (SD) for continuous variables. The KOSCHI classification was dichotomized into favorable outcomes and unfavorable outcomes for binary purposes. In detail, death, a vegetative state, and severe disability were categorized into an unfavorable group, whereas good recovery and moderate disability were categorized as favorable outcomes.[3,4]

For the development of the model, the predictors were recognized using binary logistic regression analysis. In detail, the candidate variables were identified with their $P < 0.10$ and entered into the multivariable analysis

to build the final model. All $P < 0.05$ were observed as statistically significant. Furthermore, the variance inflation factor (VIF) was analyzed in the final model for the detection of multicollinearity with a VIF value of 10 or more referring to multicollinearity.[14]

The evaluation of the model's performance comprised two domains in terms of calibration and discrimination. For calibration, the Hosmer-Lemeshow goodness-of-fit (GOF) test and the calibration plot were performed. A GOF test at a $P = 0.05$ or more indicated good calibration of the model.[15] Discrimination of the model was related to the predictability to differentiate between the binary classifiers. The concordance statistic index (C-index) or AUC were measured to indicate the discriminatory ability, while an internal validation was conducted to detect the overfitting problems of the model. Resampling techniques were used as both 1000 bootstrapping and 5-cross validation.[15,16] Finally, the model was built as a nomogram. Statistical analyses were performed using the R version 3.6.2 software (R Foundation, Vienna, Austria).

Results

Clinical and neuroimaging characteristics

A total of 104 pediatric patients diagnosed with moderate and severe TBI were included in the cohort. The mean patient age was 99.75 months (SD 59.65). There were 67 males and 37 females. Children injured as a result of road traffic accidents made up 84.6% of the cohort. A total of 48.1% of the cases were moderate TBI, whereas the GCS of 3–8 was observed in 51.9% of the cohort. The clinical characteristics are summarized in Table 1.

Neuroimaging detected skull fracture and basilar skull fracture in 30.8% and 18.3% of the samples, respectively. In

Table 1: Demographic data according to the 6 months follow-up outcome (*n*=104)

Factor	Unfavorable outcome (*n*=22)	Favorable outcome (*n*=82)	Total, *n* (%)
Gender			
Male	13 (59.1)	54 (65.9)	67 (64.4)
Female	9 (40.9)	28 (34.1)	37 (35.6)
Age group (years)			
≤2	2 (9.1)	6 (7.3)	8 (7.7)
>2	20 (90.9)	76 (92.7)	96 (92.3)
≤5	11 (50.0)	25 (30.5)	36 (34.6)
>5	11 (50.0)	57 (69.5)	68 (65.4)
Mean age-month±SD	92.85±64.22	101.52±58.73	99.75±59.65
GCS score			
9-12	1 (4.5)	49 (59.8)	50 (48.1)
3-8	21 (95.5)	33 (40.2)	54 (51.9)
Injured mechanism			
Motorcycle crash	10 (45.5)	48 (58.5)	58 (55.8)
Vehicle crash	2 (9.1)	13 (15.9)	15 (14.4)
Pedestrians injured in a traffic accident	4 (18.2)	11 (13.4)	15 (14.4)
Fall from a height	1 (4.5)	5 (6.1)	6 (5.8)
Bicycle accident	3 (13.6)	3 (3.6)	6 (5.8)
Object striking the head	2 (9.1)	2 (2.4)	4 (3.8)
Loss of consciousness	8 (36.4)	43 (52.4)	51 (49.0)
Vomiting	2 (9.1)	4 (4.9)	6 (5.8)
Hemiparesis	3 (13.6)	11 (13.4)	14 (13.5)
Scalp hematoma/laceration	13 (5.9.1)	45 (54.9)	58 (55.8)
Bleeding per nose/ear	4 (18.2)	5 (6.1)	9 (8.7)
Hypotension	15 (68.2)	9 (11.0)	24 (23.1)
Bradycardia	3 (13.6)	1 (1.2)	4 (3.8)
Seizure	2 (9.1)	9 (11.0)	11 (10.6)
Pupillary light reflex			
Fixed BE	15 (68.2)	8 (9.8)	23 (22.1)
React one eye	3 (13.6)	4 (4.9)	7 (6.7)
React both eyes	4 (18.2)	70 (85.4)	74 (71.2)
Surgery (*n*=20)			
Decompressive craniectomy	3 (13.6)	7 (8.5)	10 (9.6)
Craniotomy with clot removal	1 (4.5)	7 (8.5)	8 (7.7)
ICP monitoring	1 (4.5)	1 (1.2)	2 (1.9)

ICP: İntracranial pressure, SD: Standard deviation, GCS: Glasgow Coma Scale

addition, epidural hematoma and subdural hematoma (SDH) were common intracranial injuries. The neuroimaging findings are summarized in Table 2. A total of 19.2% of cases underwent surgery. Table 3 provides a summary of the treatment and outcome. Decompressive craniectomy was performed on ten patients, while eight children received craniotomy with clot removal operations, and an intracranial monitoring procedure was performed for two children. According to the KOSCHI categories at the hospital discharge, the mortality rate was 16.3%. A vegetative state, severe disability, moderate disability, and good recovery were 1.9%, 5.8%, 10.6%, and 65.4%, respectively. When a 6-month follow-up was performed, no further deaths were recorded. Hence, the dichotomized KOSCHI groups were composed of favorable and unfavorable subgroups as 78.8% and 21.2%, respectively, at the 6-month follow-up.

Model development

Initially, ten variables (GCS score, road traffic accident, hypotension, bradycardia, pupillary light reflex, SDH, subarachnoid hemorrhage (SAH), DAI, midline shift, and basal cistern obliteration) were selected as candidates for multivariable analysis [Table 4]. After the backward elimination procedure, the VIF of the GCS of 3–8, hypotension, pupillary light reflex, and SAH were 1.059, 1.088, 1.224, and 1.248, respectively.

Model performance and internal validation

Using the Hosmer-Lemeshow GOF test, the result of the model's calibration gave a $P = 0.89$ that indicated good calibration [Figure 1]. The domain of the model's discrimination had a C-index value of 0.931. The overfitting of the model was considered by 1000

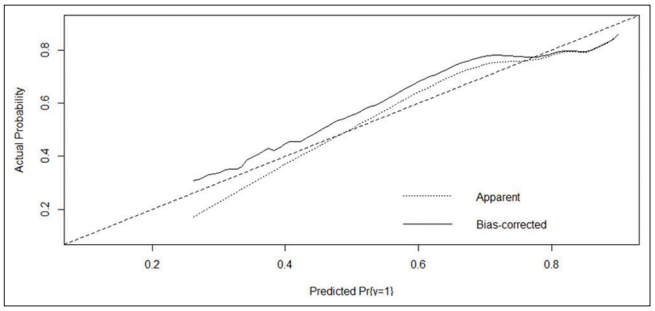

Figure 1: Calibration plot. The dashed 45° line represents the ideal performance, in which the predicted outcome corresponds acceptably to the actual performance

Table 2: Imaging findings of the present cohort (*n*=104)

Factor	Unfavorable outcome (*n*=22)	Favorable outcome (*n*=82)	Total, *n* (%)
Skull fracture	7 (31.8)	25 (30.5)	32 (30.8)
Basilar skull fracture	6 (27.3)	13 (15.9)	19 (18.3)
Epidural hematoma	5 (22.7)	23 (28.0)	28 (26.9)
SDH	12 (54.5)	25 (30.5)	37 (35.6)
Contusion	8 (36.4)	21 (25.6)	29 (27.9)
Brainstem contusion	1 (4.5)	3 (3.7)	4 (3.8)
SAH	9 (40.9)	14 (17.1)	23 (22.1)
Intraventricular hemorrhage	5 (22.7)	7 (8.5)	12 (11.5)
DAI	8 (36.4)	16 (19.5)	24 (23.1)
Midline shift (cm)			
<0.5	16 (72.7)	76 (92.7)	92 (88.5)
≥0.5	6 (27.3)	6 (7.3)	12 (11.5)
Mean of midline shift (cm)±SD	0.23±0.34	0.06±1.6	0.098±0.22
Basal cistern obliteration	10 (45.5)	11 (13.4)	21 (20.2)

SD: Standard deviation, SAH: Subarachnoid hemorrhage, SDH: Subdural hematoma, DAI: Diffuse axonal injury

Table 3: Outcome of the present cohort (*n*=104)

Factor	Unfavorable outcome (*n*=22)	Favorable outcome (*n*=82)	Total, *n* (%)
Hospital discharge KOSCHI			
Death	17 (77.3)	0	17 (16.3)
Vegetative state	2 (9.1)	0	2 (1.9)
Severe disability	3 (13.6)	3 (3.7)	6 (5.8)
Moderate disability	0	11 (13.4)	11 (10.6)
Good recovery	0	68 (82.9)	68 (65.4)
6 months follow-up KOSCHI			
Death	17 (77.3)	0	17 (16.4)
Vegetative state	2 (9.1)	0	2 (1.9)
Severe disability	3 (13.6)	0	3 (2.9)
Moderate disability	0	13 (15.9)	13 (12.5)
Good recovery	0	69 (84.1)	69 (66.3)

KOSCHI: King's Outcome Scale for Childhood Head Injury

Table 4: Binary logistic regression for the 6-month follow-up unfavorable outcome

Factor	Univariate analysis		Multivariable analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age group (years)				
≤2	Reference			
>2	0.89 (0.16-4.73)	0.89		
≤5	Reference			
>5	0.53 (0.21-1.36)	0.19		
Loss of consciousness*	0.84 (0.33-2.11)	0.72		
Vomiting*	1.72 (0.29-10.06)	0.54		
Hemiparesis*	0.89 (0.22-3.51)	0.87		
Scalp injury*	1.43 (0.56-3.65)	0.45		
Bleeding per nose/ear*	1.76 (0.40-7.64)	0.45		
Seizure*	0.71 (0.14-3.57)	0.68		
GCS score				
9-12	Reference		Reference	
3-8	36.35 (4.67-282.97)	0.001	16.07 (1.27-202.42)	0.03
Road traffic accident				
No	Reference			
Yes	3.24 (1.05-9.96)	0.03		
Hypotension	18.00 (5.87-55.153)	<0.001	19.54 (3.23-117.96)	0.001
Bradycardia	11.28 (1.11-114.12)	0.04		
Pupillary light reflex				
React both eyes	Reference		Reference	
React one eye	18.40 (3.19-105.95)	0.001	7.74 (1.26-47.29)	0.02
Fixed both eyes	25.87 (7.40-90.23)	<0.001	57.74 (2.28-145.81)	0.01
Skull fracture*	1.48 (0.57-3.87)	0.41		
Basilar skull fracture*	1.71 (0.57-5.15)	0.33		
EDH*	1.15 (0.42-3.18)	0.77		
SDH*	2.20 (0.86-5.57)	0.09		
Contusion*	1.08 (0.39-2.97)	0.87		
Brainstem contusion*	3.54 (0.47-26.62)	0.21		
IVH*	2.74 (0.78-9.61)	0.11		
SAH*	6.27 (2.25-17.43)	<0.001	9.01 (1.33-60.80)	0.02
DAI*	3.36 (1.24-9.11)	0.01		
Midline shift				
<0.5	Reference			
≥0.5	6.17 (1.74-21.83)	0.005		
Basal cistern				
Patent	Reference			
Obliteration	6.32 (2.20-18.13)	0.001		
Operation				
No surgery	Reference			
DC	1.68 (0.39-7.22)	0.48		
Craniotomy	2.36 (0.51-10.88)	0.26		
ICP monitoring	3.94 (0.23-66.28)	0.34		

*Data showed only the "yes group," while reference groups (no group) were hidden. DAI: Diffuse axonal injury, DC: Decompressive craniectomy, EDH: Epidural hematoma, GCS: Glasgow Coma Scale, ICP: İntracranial pressure, IVH: İntraventricular hemorrhage, SAH: Subarachnoid hemorrhage, SDH: Subdural hematoma, CI: Confidence interval, OR: Odds ratio

bootstrapping and 5-cross validation techniques, while the C-index values of bootstrapping and cross-validation were 0.920 and 0.924, respectively.

Model presentation

After validation, the model was presented as the final process to provide a valid prediction for new patients and then presented as a nomogram [Figure 2].

Discussion

The severity of TBI was significantly associated with the functional outcome in the cohort. The results of this study were in concordance with previous studies.[17,18] Bedry and Tadele investigated 315 children with TBI and reported that severe TBI was associated with mortality or disability compared with moderate

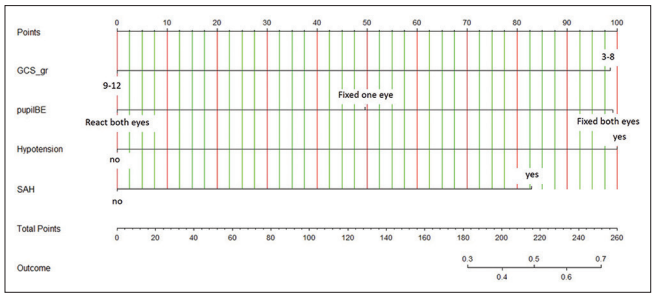

Figure 2: Predictive nomogram for the outcome of pediatric traumatic brain injury. To use the nomogram, draw a straight line upward from the patient's characteristics of the Glasgow Coma Scale (GCS_gr), pupillary light reflex (pupilBE), hypotension, and subarachnoid hemorrhage to the upper points scale for scoring each variable, and the sum of the scores of all variables. Then, draw another straight line downward from the scale of the total points through the outcome scale to measure the probability of the presence of outcome in an individual

and mild TBI (odds ratio [OR]: 2.55; 95% CI: 1.96–4.52).[17] Similarly, Kan *et al*. demonstrated that a low GCS score was significantly associated with poor outcomes in TBI children aged 2–16 years.[18] This was potentially explained by the high-energy force impacting on the head, leading to more damage of the brain parenchyma that caused a poor GCS score.[3,17,18]

Other prognostic factors in this study concurred with previous experiments.[3,19] Bahloul *et al*. reported that the prognostic factors were hypotension, bilateral mydriasis, and SAH. Bilaterally, nonreactive pupils was also one of the prognostic factors in the present study that were poor predictors as a result of the low cerebral blood flow, particularly brain stem blood flow (BBF).[20] Brain stem is the vital area of the brain where ischemic processes or infarction develop in this region that cause the dysfunction of pupillary reaction and other vital signs.[19,20] Ritter *et al*. studied BBF in severe TBI patients and found that the pupillary reaction depended on the BBF level. In detail, patients with normally reactive pupils had BBF at 30.5 ± 16.8 ml/100 g/min compared with 43.8 ± 18.7 ml/100 g/min in patients with normally reactive pupils.[20] Moreover, the presence of uncal herniation caused a marked decrease in BBF, especially in the upper brainstem,[21] while the presence of systemic hypotension significantly reduced the global cerebral blood flow.[22]

SAH was the one of the predictors in the prognostic model in the present study. From the prior studies, the presence of traumatic SAH in pediatric TBI was associated with the increased severity of the injury, while high levels required care. Hochstadter *et al*. reported the prevalence of SAH in 42% of severe pediatric TBI patients, and this injury was associated with an increased level of care requirement and increased lengths of hospital stay.[23] Dalle Ore *et al*. studied pediatric TBI patients with traumatic SAH and found that the mortality rate among all TBI children with traumatic SAH was 16.5%. Nonetheless, it still remains unclear the pathophysiology of SAH that is associated with mortality, as subsequential diffuse cerebral swelling following SAH has been discussed as a cause of a poor outcome.[24]

In this study, surgical treatment was not associated with the 6-month follow-up outcome of TBI. One limitation of a retrospective study design is the occurrence of an inherent bias that is not found in a randomized controlled trial. However, a low prevalence of moderate or severe pediatric TBI was observed in previous studies as 7.5%–29.8% for moderate TBI and 7.9%–13% for severe TBI, respectively.[3-5,25] A multicenter study or meta-analysis studies were previously conducted in an attempt to resolve this limitation, while the propensity score approach was also adopted to adjust the selection bias and non-randomized study design.[26]

Limitations

As a result, the C-index values of the nomogram, both the bootstrapping technique and cross-validation, were at an excellent level. However, the overfitting problem should be recognized and resolved by testing the prediction tool with unseen data.[27] Furthermore, the study populations were not large enough to divide the data and use the nomogram to test the performance of the unseen data. In future research, external validation would be the next step to examine the performance of the prediction tool on unseen data from subsequent patients at the same centers at which the nomogram was developed, as temporal validation or patients from centers different from those which contributed in the tool development, as geographic validation.[28]

Therefore, other limitations should be acknowledged. The nomgram was a two-dimensional graphic scoring system, which needed to assign scores to each variable that resulted in being a nonuser-friendly tool in general practice. Therefore, a web-based nomogram or mobile application should be developed and deployed to simplify the tool for the physician's practice. Moreover, the retrospective study design may lead to bias, so prospective multicenter research should also be performed in the future.

Future research directions

Various prediction tools have been performed in clinical research such as, clinical prediction rules and machine learning.[29,30] In an era of disruption, a machine learning model could be used as a clinical prediction tool to predict the outcome of various diseases.[30] Amorim *et al*. used the Naive Bayes (NB) algorithm and other machine learning algorithms to predict the mortality in patients following TBI. The NB algorithm gave an excellent performance with an AUC of 0.906, while the random forest algorithm had an AUC of 0.880.[30] Therefore, further comparative

research should be conducted using machine learning algorithms and nomograms to assess the predictability. Thus, an excellent prediction tool would have the utility for implementing a treatment strategy.

Conclusions

The clinical nomogram gave excellent performance for predicting the 6-month follow-up outcomes in pediatric TBI patients. However, further external validation is required, as a challenging future study, to compare the performance of real-world implications using other predictive algorithms.

Acknowledgment
The authors would like to offer their special thanks to Professor. Nakornchai Phuenpathom and Associate professor. Sakchai Sae-heng for their advice about manuscript preparation.

Author contributions statement
TE: Review and editing (equal), Conceptualization (supporting). TT: Conceptualization (lead); Methodology (lead); writing – original draft (lead); formal analysis (lead).

Ethical approval
All procedures performed in the study that involved studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee or both and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The study was approved by the Human Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC.63-373-10-1, Date: 29.09.2020).

Financial support and sponsorship
None.

Conflicts of interest
None Declared.

Transparency Declaration
The study population was TBI patients younger than 15 years old who underwent a CT of the brain between January 2009 and December 2018. In detail, patients diagnosed before were the study population of Tunthanathip and Phuenpathom.[7] The previous study aimed to identify predictors of intracranial injury following CT of the brain, while the present study focused on predicting the functional outcome of KOSCHI classification by nomogram.

References

1. The Lancet. The burden of traumatic brain injury in children. Lancet 2018;391:813.
2. Chaitanya K, Addanki A, Karambelkar R, Ranjan R. Traumatic brain injury in Indian children. Childs Nerv Syst 2018;34:1119-23.
3. Tunthanathip T, Phuenpathom N. Impact of road traffic injury to pediatric traumatic brain injury in Southern Thailand. J Neurosci Rural Pract 2017;8:601-8.
4. Fulkerson DH, White IK, Rees JM, Baumanis MM, Smith JL, Ackerman LL, *et al*. Analysis of long-term (median 10.5 years) outcomes in children presenting with traumatic brain injury and an initial Glasgow Coma Scale score of 3 or 4. J Neurosurg Pediatr 2015;16:410-9.
5. Phuenpathom N, Tiensuwan M, Ratanalert S, Saeheng S, Sripairojkul B. The changing pattern of head injury in Thailand. J Clin Neurosci 2000;7:223-5.
6. Kavosi Z, Jafari A, Hatam N, Enaami M. The economic burden of traumatic brain injury due to fatal traffic accidents in Shahid Rajaei trauma hospital, Shiraz, Iran. Arch Trauma Res 2015;4:e22594.
7. Tunthanathip T, Ratanalert S, Sae-Heng S, Oearsakul T, Sakaruncchai I, Kaewborisutsakul A, *et al*. Prognostic factors and nomogram predicting survival in diffuse astrocytoma. J Neurosci Rural Pract 2020;11:135-43.
8. Tunthanathip T, Udomwitthayaphiban S. Development and validation of a nomogram for predicting the mortality after penetrating traumatic brain injury. Bull Emerg Trauma 2019;7:347-54.
9. Mongkornwong A, Sangthong R, Tunthanathip T, Sangkhathat S. Factors associated with in-hospital mortality in severe burn patients in Songklanagarind hospital: A retrospective Study. J Health Sci Med Res 2021;40:1-10.
10. Cappellari M, Turcato G, Forlivesi S, Bagante F, Cervellin G, Lippi G, *et al*. The START nomogram for individualized prediction of the probability of unfavorable outcome after intravenous thrombolysis for stroke. Int J Stroke 2018;13:700-6.
11. Parmontree P, Tunthanathip T, Doungngern T, Rojpitbulstit M, Kulviwat W, Ratanalert S. Predictive risk factors for early seizures in traumatic brain injury. J Neurosci Rural Pract 2019;10:582-7.
12. Thai Thanh Truc. Statistics and Sample Size Pro. Web site. Available from: https://play.google.com/store/apps/details?id=thaithanhtruc.info.stat&hl=en_US&gl=US. [Last cited on 2020 Mar 15].
13. Vieira RC, Paiva WS, de Oliveira DV, Teixeira MJ, de Andrade AF, de Sousa RM. Diffuse axonal injury: Epidemiology, outcome and associated risk factors. Front Neurol 2016;7:178.
14. Vatcheva KP, Lee M, McCormick JB, Rahbar MH. Multicollinearity in regression analyses conducted in epidemiologic studies. Epidemiology (Sunnyvale) 2016;6:227.
15. Han K, Song K, Choi BW. How to develop, validate, and compare clinical prediction models involving radiological parameters: Study design and statistical methods. Korean J Radiol 2016;17:339-50.
16. Austin PC, Tu JV. Bootstrap methods for developing predictive models. Am Stat 2004;58:131-7.
17. Bedry T, Tadele H. Pattern and outcome of pediatric traumatic brain injury at hawassa university comprehensive specialized hospital, Southern Ethiopia: Observational cross sectional study. Emerg Med Int 2020;2020:1-9.
18. Kan CH, Saffari M, Khoo TH. Prognostic factors of severe traumatic brain injury outcome in children aged 2-16 years at a major neurosurgical referral centre. Malays J Med Sci 2009;16:25-33.
19. Bahloul M, Ben Hamida C, Chelly H, Chaari A, Kallel H, Dammak H, *et al*. Severe head injury among children: prognostic factors and outcome. Injury 2009;40:535-40.
20. Ritter AM, Muizelaar JP, Barnes T, Choi S, Fatouros P, Ward J, *et al*. Brain stem blood flow, pupillary response, and outcome in patients with severe head injuries. Neurosurgery 1999;44:941-8.
21. Vathanalaoha K, Oearsakul T, Tunthanathip T. Predictive factors of survival and 6-month favorable outcome of very severe head trauma patients; a historical cohort study. Emerg (Tehran) 2017;5:e24.
22. Duschek S, Schandry R. Reduced brain perfusion and cognitive performance due to constitutional hypotension. Clin Auton Res 2007;17:69-76.
23. Hochstadter E, Stewart TC, Alharfi IM, Ranger A, Fraser DD. Subarachnoid hemorrhage prevalence and its association with short-term outcome in pediatric severe traumatic brain injury. Neurocrit Care 2014;21:505-13.
24. Dalle Ore CL, Rennert RC, Schupper AJ, Gabel BC, Gonda D, Peterson B, *et al*. The identification of a subgroup of children

with traumatic subarachnoid hemorrhage at low risk of neuroworsening. J Neurosurg Pediatr 2018;22:559-66.

25. Taweesomboonyat T, Kaewborisutsakul A, Tunthanathip T, Saeheng S, Oearsakul T. Necessity of in-hospital neurological observation for mild traumatic brain injury patients with negative computed tomography brain scans. J Health Sci Med Res 2000;38:267-74.
26. Austin PC, van Klaveren D, Vergouwe Y, Nieboer D, Lee DS, Steyerberg EW. Geographic and temporal validity of prediction models: Different approaches were useful to examine model performance. J Clin Epidemiol 2016;79:76-85.
27. Roelen CA, Bültmann U, van Rhenen W, van der Klink JJ, Twisk JW, Heymans MW. External validation of two prediction models identifying employees at risk of high sickness absence: Cohort study with 1-year follow-up. BMC Public Health 2013;13:105.
28. Austin PC, van Klaveren D, Vergouwe Y, Nieboer D, Lee DS, Steyerberg EW. Validation of prediction models: Examining temporal and geographic stability of baseline risk and estimated covariate effects. Diagn Progn Res 2017;1:12.
29. Stein SC, Attiah MA. Clinical prediction and decision rules in neurosurgery: A critical review. Neurosurgery 2015;77:149-55.
30. Amorim RL, Oliveira LM, Malbouisson LM, Nagumo MM, Simoes M, Miranda L, *et al*. Prediction of early TBI mortality using a machine learning approach in a LMIC population. Front Neurol 2019;10:1366.