Application of machine learning to predict the outcome of pediatric traumatic brain injury

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**ABSTRACT**

**Purpose:** Traumatic brain injury (TBI) generally causes mortality and disability, particularly in children. Machine learning (ML) is a computer algorithm, applied as a clinical prediction tool. The present study aims to assess the predictability of ML for the functional outcomes of pediatric TBI.

**Methods:** A retrospective cohort study was performed targeting children with TBI who were admitted to the trauma center of southern Thailand between January 2009 and July 2020. The patient was excluded if he/she (1) did not undergo a CT scan of the brain, (2) died within the first 24 h, (3) had unavailable complete medical records during admission, or (4) was unable to provide updated outcomes. Clinical and radiologic characteristics were collected such as vital signs, Glasgow coma scale score, and characteristics of intracranial injuries. The functional outcome was assessed using the King’s Outcome Scale for Childhood Head Injury, which was thus dichotomized into favourable outcomes and unfavourable outcomes: good recovery and moderate disability were categorized as the former, whereas death, vegetative state, and severe disability were categorized as the latter. The prognostic factors were estimated using traditional binary logistic regression; hence, the 4 prognostic factors were used for building ML models and testing performance.

**Results:** There were 828 patients in the cohort. The median age was 72 months (interquartile range 104.7 months, range 2–179 months). Road traffic accident was the most common mechanism of injury, accounting for 68.7%. At hospital discharge, favourable outcomes were achieved in 97.0% of patients, while the mortality rate was 2.2%. Glasgow coma scale score, hypotension, pupillary light reflex, and subarachnoid haemorrhage were associated with TBI outcomes following traditional binary logistic regression; hence, the 4 prognostic factors were used for building ML models and testing performance. The support vector machine model had the best performance for predicting pediatric TBI outcomes: sensitivity 0.95, specificity 0.60, positive predicted value 0.99, negative predicted value 1.0; accuracy 0.94, and area under the receiver operating characteristic curve 0.78.

**Conclusion:** The ML algorithms of the present study have a high sensitivity; therefore they have the potential to be screening tools for predicting functional outcomes and counselling prognosis in general practice of pediatric TBIs.

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**Introduction**

Traumatic brain injury (TBI) in children is a public health problem. From previous studies in Thailand, 37.5%–65.3% of pediatric TBIs were injured from road traffic accidents and 22.4% of the wounded was motorcycle drivers. The mortality rate of pediatric TBIs of all ranges of severity has been reported at 3.2%–5.2%, while 0.3%–0.8% of those were found as a vegetative state and...
severe disability. More than half of severe pediatric TBIs died within one year after injuries, and only 4.6%–8.7% had a good recovery.

Post-traumatic sequelae and long-term consequences of severe pediatric TBIs have been recognized to incur a productivity loss for the nation. Prediction of functional outcomes among the injured children is one of the important processes to evaluate future economic burden. In general, the clinical outcome is predicted from independent variables by traditional statistical methods. Nowadays, machine learning (ML) algorithms have been used as clinical prediction tools in the literature. Prior studies have performed ML for classifying and predicting clinical outcomes such as neuro-oncology, TBI, stroke, and postoperative complications.

The ML approach, particularly supervised ML, has also been used to predict clinical outcomes following TBI. Random forest has been reported as a valuable method for predicting moderate to severe TBIs based on quantitative electroencephalography measurements and clinical parameters, which has an area under the receiver operating characteristic curve (AUC) of 0.94–0.81 according to the study of Haveman et al. In addition, the performance of mortality prediction in TBIs reported that the models of random forest, support vector machines, neural networks, and gradient boosting machines have an AUC of 0.81 (95% CI 0.78–0.84), 0.81 (95% CI 0.79–0.84), 0.82 (95% CI 0.79–0.84), and 0.83 (95% CI 0.81–0.86), respectively. Amorim et al. used various ML algorithms to predict the mortality of TBI patients and found that the naive Bayes algorithm had the best predictive value of mortality (AUC = 0.906), while random forest had an AUC of 0.880. The concordance of the results demonstrated that naive Bayes had the best performance for predicting clinical outcomes, but an AUC equal to 0.76 was not a good performance. In the face of this gap, we aimed to evaluate the predictive performance of ML algorithms for clinical outcomes. Also, the present study is based on the functional outcomes of pediatric TBI.

**Methods**

**Study design and study population**

The authors retrospectively reviewed the medical records of patients with TBI admitted to the trauma center of southern Thailand, who were younger than 15 years between January 2009 and July 2020. In detail, all TBI patients had been prospectively registered in the traumatic database of our hospital. The exclusion criteria were patients who did not undergo a CT scan of the brain, died within the first 24 h, had unavailable complete medical records during admission and those who were unable to provide the updated outcomes.

Various clinical, radiological, treatment and outcome variables were collected for analysis. Glasgow coma scale (GCS) score after resuscitation was used to classify TBI severity: mild TBI (GCS score 13–15), moderate TBI (GCS score 9–12), and severe TBI (GCS score 3–8). In addition, secondary systemic injuries such as hypotension and bradycardia were defined according to the age period. Radiological findings, the characteristics of intracranial injuries, midline shift, and obliteration of basal cistern were reviewed by two neurosurgeons. Based on Vieira et al., the diffuse axonal injury was defined where patients had a GCS score of ≤8 following resuscitation and CT scan or MRI showed signs of diffuse axonal injury.

The functional outcome of the present study was assessed using King’s Outcome Scale for Childhood Head Injury (KOSCHI). The KOSCHI classification was collected at hospital discharge and every follow-up visit. For patients who were unable to follow up face to face, we evaluated the patients’ outcomes by telephone. Patients who could not be contacted were excluded. For the dependent variable, the KOSCHI classification was dichotomized into favourable outcomes and unfavourable outcomes for binary proposes. Good recovery and moderate disability were categorized as favourable outcomes, whereas death, vegetative state, and severe disability were categorized into the unfavourable group.

The study was performed with the approval of the human research ethics committee (REC.63-373-10-1). Because the present study was a retrospective cohort study design, informed consent was not performed. However, the patients’ identification numbers were encoded before analysis.

**Statistical analysis**

Clinical characteristics were calculated from descriptive data. The median with interquartile range (IQR) was used for continuous variables. The prognostic variables, which were used for building the ML models, were analyzed using the traditional binary logistic regression. Initially, clinical and imaging variables were estimated by univariate analysis and the variables that had p values less than 0.01 were regarded as candidate variables. In multivariable analysis, these candidate variables were estimated whether they should be included as the prognostic factors using the Akaikie information criterion. Thereafter the qualified prognostic factors were used for building ML models. In this part, statistical analysis was performed using the R version 3.6.2 software (R Foundation, Vienna, Austria).

**ML**

By randomly splitting data, 70% of the total data were used to train the ML models, while the remaining 30% were used for testing the models’ performance. Data preprocessing included dichotomization of independent variables into binary classifiers. Because patients who had incomplete data were excluded, missing data management was not performed in the present study.

Supervised algorithms with 10-fold cross-validation including support vector machines, neural networks, naive Bayes, logistic regression, and k-nearest neighbor were used for training the models from the training dataset. The parameters of each algorithm were also optimized by the grid-search method. Therefore, a confusion matrix was constructed to describe the performance of ML models for which the true values of the outcome were known. To test the ML models, we built web-based applications of various algorithms using stream lit and deployed via the Heroku platform.

**Results**

**Clinical and radiological characteristics**

A total of 828 patients were included in the present cohort. Median patient age was 72 months (IQR 104.7 months, range 2–179 months). There were 567 males and 261 females. The mechanisms of TBIs included motorcycle crashes (51.0%), falls (25.7%),
pedestrians injured in traffic accidents (9.1%), objects striking the head (2.9%), vehicle accidents (8.7%) and bicycle accidents (2.7%). After resuscitation, 87.4% of the cases were of mild TBI (GCS 13–15), while moderate and severe TBI were found in 6.0% and 6.5% of patients, respectively. A summary of the demographic data is presented in Table 1. Long bone fractures and maxillofacial injuries were the most common associated injuries, whereas coagulopathy was found in 0.4% in the present cohort. Additionally, the post-traumatic seizure was observed in 5.0% of cases (Table 1).

From the radiological findings, intracranial injuries were observed as follows: skull fracture (14.6%), basilar skull fracture (4.8%), epidural hematoma (8.3%), subdural hematoma (11.7%), contusion (7.6%), brainstem contusion (0.5%), subarachnoid haemorrhage (5.8%), and primary intraventricular haemorrhage (1.6%). Moreover, a diffuse axonal injury was diagnosed in 2.9% of cases. The radiological findings and outcomes are revealed in Table 2.

| Variables | n (%) |
|-----------|-------|
| Age (years) | |
| <2 | 119 (14.4) |
| ≥2 | 709 (85.6) |
| Age (years) | |
| <5 | 335 (40.5) |
| ≥5 | 493 (59.5) |
| Median age (IQR) (months) | 72 (104.7) |
| Gender | |
| Male | 567 (68.5) |
| Female | 261 (31.5) |
| Mechanism of injury | |
| Motorcycle crash | 422 (51.0) |
| Fall | 213 (25.7) |
| Pedestrians injured | 75 (9.1) |
| Vehicle crash | 72 (8.7) |
| Object striking the head | 24 (2.9) |
| Bicycle accident | 22 (2.7) |
| Mean injury severity score (SD) | 21.5 (7.9) |
| Association of injuries | |
| Long bone fracture | 165 (19.9) |
| Maxillofacial injury | 82 (9.9) |
| Orbital injury | 44 (5.3) |
| Lung contusion | 39 (4.7) |
| Liver injury | 30 (3.6) |
| Spine fracture | 30 (3.6) |
| Kidney, ureter, and bladder injury | 21 (2.5) |
| Spinal injury | 18 (2.2) |
| Pelvic fracture | 17 (2.0) |
| Bowel injury | 8 (0.9) |
| Retroperitoneal injury | 7 (0.8) |
| Comorbidities | |
| Scalp hematoma/laceration | 487 (58.8) |
| Loss of consciousness | 315 (38.0) |
| Anemia | 225 (27.2) |
| Vomiting | 210 (25.4) |
| Seizure | 41 (5.0) |
| Hypotension episode | 34 (4.1) |
| Bleeding per ear/nose | 22 (2.7) |
| Hemiparesis | 21 (2.5) |
| Bradycardia | 6 (0.7) |
| Coagulopathy | 3 (0.4) |
| Glasgow coma scale score | |
| 13-15 | 724 (87.4) |
| 9-12 | 50 (6.0) |
| 3-8 | 54 (6.5) |
| Pupillary light reflex | |
| Fixed pupils both eyes | 24 (2.9) |
| Fixed pupil one eyes | 16 (1.9) |
| React pupils both eyes | 788 (95.2) |

| Variables | n (%) |
|-----------|-------|
| Skull fracture | 121 (14.6) |
| Linear skull fracture | 70 (8.5) |
| Simple depressed skull fracture | 20 (2.4) |
| Compound depressed skull fracture | 19 (2.3) |
| Diastatic skull fracture | 12 (1.4) |
| Intracranial injuries | |
| Basilar skull fracture | 40 (4.8) |
| Epidural hematoma | 69 (8.3) |
| Subdural hematoma | 97 (11.7) |
| Contusion | 63 (7.6) |
| Brainstem contusion | 4 (0.5) |
| Subarachnoid haemorrhage | 48 (5.8) |
| Intraventricular haemorrhage | 13 (1.6) |
| Diffuse axonal injury | 24 (2.9) |

KOSCHI categories at hospital-discharge included death (2.2%), vegetative state (0.2%), severe disability (0.7%), moderate disability (1.6%), and good recovery (95.3%). At 6-month follow-up, the rates of death, vegetative state, severe disability, moderate disability, and good recovery were 2.2%, 0.2%, 0.4%, 1.8%, 95.4%, respectively. Therefore, the dichotomized KOSCHI categories comprised of 97.0% favourable and 3.0% unfavourable outcomes after hospital discharge (Table 2).

When clinical and imaging characteristics were estimated for the prognostic variables using the traditional binary logistic regression, GCS score, hypotension, pupillary light reflex, and subarachnoid haemorrhage were found to be prognostic variables in the final model, as shown in Table 3. Hence, these prognostic variables were used for supervised learning.

| ML | |
| After splitting the data, 580 patients were considered suitable for the training dataset and were used to construct the ML models. The parameters of the ML models were optimized using the grid search method. In detail, the support vector machines model was optimized with a linear kernel, scale grama and the regularization parameter (C parameter) of 1.0, while the optimized logistic regression model was C parameter of 0.10 with “l2” penalization. Optimization of the neural networks model comprised of two hidden layers, “identity” activation, “lbfgs” “solver”, “invasive” learning and an alpha of 0.0001. For k-nearest neighbor, the model parameters were optimized with a linear kernel, scale grama and the regularization parameter (C parameter) of 1.0, while the optimized logistic regression model was C parameter of 0.10 with “l2” penalization.
was also optimized with 5 neighbors and uniform weight function. Additionally, the optimized random forest model comprised 5 maximum depths of the tree with 1000 trees in the forest.

Almost all the ML models had excellent performances after training. Support vector machines, neural networks, and logistic regression were the best models with high sensitivity and PPV. Thus, details of performances from the training data are shown in Table 4. Moreover, support vector machines had a sensitivity of 0.95, specificity 0.60, PPV 0.99, NPV 0.21, and accuracy 0.94, whereas the neural networks model had the sensitivity of 0.84, specificity 0.60, PPV 0.98, NPV 0.07 and accuracy 0.83. In addition, various ML models were built in the web-based applications for testing further unseen data (https://pedtbi-home.herokuapp.com).

For testing the ML models, AUC of all the algorithms decreased. However, the support vector machines model and the neural networks model still had AUC in acceptable levels at 0.78 and 0.72, while the AUC of other ML models dropped to less than 0.7, as shown in Fig. 1. Moreover, support vector machines had a sensitivity of 0.95, specificity 0.60, PPV 0.99, NPV 0.21, and accuracy 0.94, whereas the neural networks model had the sensitivity of 0.84, specificity 0.60, PPV 0.98, NPV 0.07 and accuracy 0.83. In addition, various ML models were built in the web-based applications for testing further unseen data (https://pedtbi-home.herokuapp.com).

### Discussion

A favourable outcome was reported to be 84.2%–99.2% in pediatric TBI patients in the literature.19,21 Hawley et al.19 studied the

### Table 3

Traditional binary logistic regression for favourable outcome.

| Variables                  | Univariate analysis | Multivariable analysis |
|----------------------------|---------------------|------------------------|
|                            | Odds ratio (95% CI) | p value                |
|                            | Odds ratio (95% CI) | p value                |
| Age group (years)          |                     |                        |
| <2                        | Ref                 |                        |
| ≥2                        | 1.12 (0.21–5.95)    | 0.89                   |
| Age group (years)          |                     |                        |
| <5                        | Ref                 |                        |
| ≥5                        | 1.86 (0.73–4.72)    | 0.19                   |
| Road traffic injury        | No                  |                        |
|                           | Ref                 |                        |
|                           | Yes                 | 0.96 (0.41–2.26)       | 0.93                   |
| Comorbidities              |                     |                        |
| Loss of consciousnessa    | 0.65 (0.29–1.45)    | 0.30                   |
| Vomiting                   | 4.02 (0.94–17.19)   | 0.06                   |
| Hemiparesisa               | 0.14 (0.03–0.36)    | <0.001                 |
| Scalp injury               | 0.79 (0.34–1.82)    | 0.59                   |
| Bleeding per nose/eara     | 0.17 (0.04–0.64)    | 0.009                  |
| Seizure                    | 0.58 (0.13–2.58)    | 0.48                   |
| Hypotension                | 0.01 (0.004–0.02)   | <0.001                 |
| Bradycardia                | 0.02 (0.005–0.14)   | <0.001                 |
| Injury severity score      | 0.14 (0.14–2.36)    | 0.56                   |
| Glasgow coma scale score   | 2.04 (1.68–2.49)    | <0.001                 |
| Fixed both eyes            |                      |                        |
| React one eye              | 5.0 (1.23–20.30)    | 0.02                   |
| React both eyes            | 21.7 (6.68–68.7)    | <0.001                 |
| Intracranial injuries      |                      |                        |
| Skull fracturea            | 0.23 (0.10–0.53)    | 0.001                  |
| Basilar skull fracturea    | 0.14 (0.05–0.37)    | <0.001                 |
| Epidural hematomaa         | 0.21 (0.08–0.53)    | 0.001                  |
| Subdural hematomaa         | 0.10 (0.04–0.23)    | <0.001                 |
| Contusion                  | 0.15 (0.06–0.37)    | <0.001                 |
| Brainstem contusiona       | 0.02 (0.004–0.21)   | 0.001                  |
| Intraventricular haemorrhage | 0.04 (0.01–0.13) | <0.001                 |
| Subarachnoid haemorrhagea  | 0.04 (0.01–0.09)    | <0.001                 |
| Diffuse axonal injurya     | 0.02 (0.01–0.06)    | <0.001                 |
| Midline shift (mm)         |                      |                        |
| <0.5                      | Ref                 |                        |
| ≥0.5                      | 0.01 (0.005–0.05)   | <0.001                 |
| Basal cistern              |                      |                        |
| Obliteration               | Ref                 |                        |
| Patent                     | 5.17 (0.13–7.17)    | 0.98                   |

* Data only show “yes group” while reference groups (no group) are hidden.

### Table 4

Performances of each algorithm to predict outcome using training data (n = 580).

| Algorithm                  | Sensitivity | Specificity | PPV | NPV | Accuracy score (SD) | F1-score (SD) | Mean AUC (SD) |
|----------------------------|-------------|-------------|-----|-----|---------------------|--------------|---------------|
| Support vector machines    | 0.99 (0.98–1.00) | 0.71 (0.37–1.00) | 0.99 (0.98–1.00) | 0.71 (0.37–1.00) | 0.90 (0.0254) | 0.50 (0.33) | 0.98 (0.04) |
| Neural networks            | 0.99 (0.98–1.00) | 0.71 (0.37–1.00) | 0.99 (0.98–1.00) | 0.83 (0.53–1.00) | 0.93 (0.14) | 0.61 (0.30) | 0.99 (0.02) |
| Logistic regression        | 0.99 (0.98–1.00) | 0.57 (0.20–0.93) | 0.98 (0.97–1.00) | 0.66 (0.28–1.00) | 0.93 (0.14) | 0.61 (0.30) | 0.98 (0.03) |
| k-nearest neighbor         | 0.98 (0.97–1.00) | 0.57 (0.20–0.93) | 0.98 (0.97–1.00) | 0.57 (0.20–0.93) | 0.93 (0.15) | 0.47 (0.38) | 0.89 (0.16) |
| Naive Bayes                | 0.95 (0.93–0.98) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 0.95 (0.93–0.98) | 0.89 (0.27) | 0.75 (0.28) | 0.95 (0.11) |
| Random forest              | 0.99 (0.98–1.00) | 0.85 (0.59–1.00) | 0.92 (0.98–1.00) | 0.85 (0.59–1.00) | 0.91 (0.21) | 0.55 (0.36) | 0.97 (0.08) |

Abbreviation: AUC: area under the curve, NPV: negative predictive value, PPV: positive predictive value. 

* 10-fold cross-validation.
outcome of 526 children with TBI and found that the rates of good recovery and moderate disability were 51.3% and 47.9%, respectively; while another prior study reported a good recovery of 94% and moderate disability of 1.7% among 948 pediatric TBI patients. In the present cohort, we found an overall favourable outcome of 96.9%. The severity of TBIs, which is categorized by the GCS score, is well known as a TBI predictor, including TBIs in children. Bredy et al. studied 315 children with TBIs and reported that severe TBIs were associated with mortality or disability compared with moderate and mild TBIs (odds ratio (OR) 2.55, 95% CI 1.96–4.52). Additionally, a previous study used the traditional binary logistic regression for identifying prognostic factors significantly associated with unfavourable outcomes as follows: GCS score 3–8, hemiparesis, pupillary light reflex, hypotension, basilar skull fracture, epidural hematoma, subdural hematoma, and motorcycle crash mechanism.5

When traditional binary logistic regression was performed with a backward elimination procedure, the prognostic factors were GCS score, hypotension, pupillary light reflex, and subarachnoid hae-
morrhage. These clinical characteristics have been reported in previous studies as prognostic factors. Hypotension meaningfully increased the mortality and poor outcome in pediatric TBIs, which could be explained by the systematic hypoperfusion directly effecting the global cerebral ischemia.22,23 Low GCS scores and poor pupillary light reflex have been associated with poor outcomes and low survival rate.4,5,12 because these factors indicate the severity of TBI and brainstem dysfunction.25 In addition, subarachnoid hemorrhage is one of the prognostic factors in the present study. However, this result differed from a prior study by Hochstadter et al. who studied 171 pediatric severe TBIs and reported that subarachnoid hemorrhage was not significantly associated with mortality in multivariable analysis. Nevertheless, there is a lack of studies that mention the relation of imaging findings with prognosis in pediatric TBIs. This topic needs further studies to explore the controversial results.

For ML-based prediction, prognostic factors were used for developing the model with various algorithms. We observed the overfitting performances during the model training, therefore the application of the model with the testing datasets resolved the problem. The support vector machines algorithm was achieved and validated with the test dataset. From a literature review, various ML algorithms have been performed as clinical prediction tools. Gravesteijn et al. studied the prognostication of TBI patients using the algorithms of random forest, support vector machines, neural networks, and gradient boosting machines and the AUCs of all of them were at a good level. Moreover, Amorim et al. built the ML-based model for mortality of TBIs in Brazil and found that AUCs of naïve Bayes, Bayesian generalized linear model, random forest, and penalized discriminant analysis were of high values of 0.906, 0.881, 0.880, and 0.880, respectively.

In the present study, the support vector machines and neural networks algorithms had acceptable performances in predicting the functional outcome following pediatric TBIs, with a particularly high sensitivity. For implication, these ML algorithms may be involved in general practice as the screening tools for counselling parents about prognosis. Stromberg et al. performed the ML-based prediction for employment following moderate to severe TBIs. AUCs of the decision tree model was 0.77 (95% CI 0.74–0.80) and 0.72 (95% CI 0.68–0.76) for 1-year and 5-year outcomes, respectively. Moreover, the predictability of surgical site infection in neurological operation using various ML algorithms and the naïve Bayes algorithm had the highest AUC of 0.76, sensitivity 0.63, specificity 0.87, PPV 0.29, NPV 0.96, and accuracy 0.86.13

ML algorithms had varying performances for predicting clinical outcomes. The characteristics of the study population possibly explain this. The type of predictors such as continuous variables and categorized variables (GCS score and severity of TBIs) affects the predictability of ML models.13 In addition, a number of predictors were associated with high performance.28,29 More significant predictors and more high-dimensional data increased the performance of ML.30,31 Moreover, because several ML algorithms are flexible from hyperparameters adjustment, the performance of each algorithm was considerably dependent on its hyperparameters.15

Limitations of the present study are acknowledged that study design was a retrospective cohort study which might have led to bias from confounding factors. The multivariable analysis helps to control this bias, but the number of parameters for building the ML model is limited after adjustment with multivariable analysis. Additionally, the imbalance among the severity of TBI was probably why performance reached an excellent level and high sensitivity. Because a limited number of moderate and severe TBI was observed in the present cohort, a multicenter-study may be able to resolve this problem for improving the predictive performance. Also, the predictability of the ML models of the present study needs to be confirmed by external validation with unseen data in the future. Alternatively, a nomogram is one of the clinical prediction tools that have been performed for predicting the outcome of various diseases.6–14 Therefore, researches should be explored in the future with a comparison of predictability between ML-based models and nomogram.

In summary, we found that ML algorithms have a high sensitivity and PPV; therefore, ML models had the potential performance as a screening tool for predicting the functional outcome in pediatric TBIs for real-world implication.

Transparency declaration

This research was a part of a retrospective cohort study that will be published elsewhere, whereas this study focused on application of machine learning to predict the outcome of pediatric traumatic brain injury.

Fig. 1. Receiver operating characteristic curve and AUC of various algorithms to predict the outcomes following pediatric traumatic brain injury from the testing dataset. AUC: area under the curve, kNN: k-nearest neighbor, LR: Logistic regression, NB: naive Bayes, NN: Neural networks, RF: random forest, SVM: support vector machine.
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