Validation of a new prognostic model in patients with severe traumatic brain injury : a multicenter observational study

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Introduction: We previously established and reported a new mathematical prognostic model for severe traumatic brain injury (Acute Medicine & Surgery, 2014). The purpose of the present study was to validate our prediction model and compared the predictive value to previously established models.

Methods: One hundred and nine patients with a Glasgow Coma Scale score of <9 were enrolled in this multicenter cohort study consisting of four tertiary critical care medical centers in Japan. Our prognostic model included the variables of age, pupillary light reflex on admission, intracranial pressure on ICU admission, subarachnoid hemorrhage and midline shift on CT scan within 24 hours of injury. Outcome was assessed prospectively 6 months after injury according to the Glasgow Outcome Scale. GR and MD were considered to be favorable outcomes. SD, PVS, and D were considered unfavorable. The predictive accuracy was compared to the two models derived from International Mission for Prognosis and Analysis of Clinical Trials in traumatic brain injury (IMPACT) or Corticosteroid Randomization After Significant Head Injury (CRASH).

Results: Out of 109 patients, 25 (22.9%) had favorable outcome, and 84 (77.1%) had unfavorable outcome. The area under the receiver operating characteristic curve of our model was 0.813. That of IMPACT and CRASH was 0.768 and 0.787, respectively. If a cut-off value was imposed according to Youden index for each model, the positive predictive value and specificity of our model were higher than the other models, but negative predictive value and sensitivity were lower compered to the two models.

Conclusion: Our prognostic model was shown to have high predictive value on external validation, and was equivalent to IMPACT or CRASH models in predictive accuracy. It will be useful for family counseling and review of treatment in patients with severe traumatic brain injury.

Background and Objective

Severe traumatic brain injury (TBI) is a leading cause of death and severe disability. Outcome prediction is useful for decision-making of treatment strategy, family counseling, evaluation of treatment effectiveness, efficient use of limited medical resources. Although numerous investigators have proposed prognostic models for TBI, a mathematical model with high predictive value has not yet been established.

Previously, we established and reported a new mathematical prognostic model for severe TBI (Acute Medicine & Surgery, 2014). According to the cross validation, our predictive model was shown to have high predictive value, but was not yet validated externally.

The purpose of the present study was to validate our prediction model externally, and compared the predictive value to previously established models.

Methods

One hundred and nine patients with a Glasgow Coma Scale (GCS) score of <9 within 12 hours after injury were enrolled in this multicenter cohort study consisting of four tertiary critical care medical centers in Japan.

All patients received the same initial standardized treatment protocol, which included appropriate resuscitation and stabilization in accordance with the Advanced Trauma Life Support Guidelines and immediate neurologic evaluation (GCS score, pupil size and reactivity, and neurological deficits). Patients were examined by computed tomography (CT) as soon after stabilization as possible. An intracranial pressure (ICP) monitor was inserted in each patient.

Grade and definition of collected variables are shown in Table 1. Absent cisterns was defined as absence of the basal cisterns including the suprasellar cisterns, ambient cisterns, and quadrigeminal cisterns. Extensive traumatic subarachnoid hemorrhage (Ext-SAH) was defined as the presence of a high density area both in the basal cisterns and over the convexity on the CT scan. Midline shift was measured at the level of the septum pellucidum.

Our predictive model is as below :

Pu = exp (B) / 1+exp (B)

Pu ; probability of an unfavorable outcome
Exp (B) ; exponential function of B
B = 0.069 * age (years) + 0.042 * ICP (mmHg) + 0.084 * midline shift (mm) + 2.481 * ext-SAH (1 or 0) – 1.852 * LR (1 or 0) – 3.098

In all cases, the outcome was assessed prospectively at 6 months after injury according to the Glasgow Outcome Scale. Good recovery and moderate disability were considered to be favorable outcomes. Severe disability , persistent vegetative state, and death were considered unfavorable.

Statistical analyses were carried out using JMP Pro 10.0.2 for Macintosh (SAS Institute, Cary, NC, USA) and Prism 6.0e for Mac (GraphPad Software, La Jolla, CA, USA).

The predictive accuracy was compared to the two models derived from International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) or Corticosteroid Randomization After Significant Head Injury (CRASH).

Table 1. Grade and definition of Variables

Variable	Grades and Definition
Age	Years
Sex	Male of Female
GCS score	3-15
LR	1: Bi/unilaterally persent
	0: Bilaterally absent
ICP	mmHg
CPP	mmHg
BD	mEq/L
Hypoxia	PaO2 <60mmHg
Hypocapsia	PaCO2 <35mmHg
Hypercapsia	PaCO2 >45mmHg
Hypotension	Systolic blood pressure <90mmHg
Absent cisterns	0: Basal cistern present
	1: Basal cistern absent
Midline shift	Mm
Ext-SAH	0: Absent
	1: Present
Body temperature	°C
Glucose	mg/dL
Hemoglobin	g/dL
Epidural hematoma	No or Yes
Petechial hemorrhage	No or Yes
Non-evacuated hematoma	No or Yes
Major extra-cranial injury	No or Yes

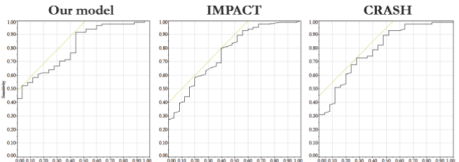
GCS: Glasgow Coma Scale, BD: base deficit, LR: pupillary light reflex, ICP: intracranial pressure, CPP: cerebral perfusion pressure, Ext-SAH: extensive subarachnoid hemorrhage

Table 2. Patient characteristics

Number of cases	109
Age	7-89 (median 51)
Sex (male : female)	82 : 27
GCS on admission	3-15
Number of bilaterally absent of LR	36 (33.0%)
Body temperature	34.1-37.6 (median 35.8)
Glucose	94-350 (median 178)
Hemoglobin	5.1-18.4 (median 13.1)
ICP	0-120 (median 16.5)
CPP	5-124 (median 60)
Number of Hypoxia	9 (8.3%)
Number of Hypocapsia	23 (21.1%)
Number of Hypercapnia	27 (24.8%)
Number of Hypotension	8 (7.3%)
TCDB CT classification	
Diffuse Injury I	1 (0.9%)
Diffuse Injury II	24 (22.0%)
Diffuse Injury III	6 (5.5%)
Diffuse Injury IV	3 (2.8%)
Evacuated Mass Lesion	66 (60.6%)
Non-evacuated Mass Lesion	9 (8.3%)
Midline shift	0-33.4 (median 7.1)
Number of Absent cisterns	30 (27.5%)
Number of ext-SAH	77 (70.6%)
Number of epidural hematoma	29 (26.9%)
Number of petechial hemorrhage	85 (78.7%)
Number of non-evacuated hematoma	9 (8.3%)
Number of major extra-cranial injury	58 (53.2%)
Pu	0.036-0.999 (median 0.930)

Pu: Probability of an unfavorable outcome

Figure 1. Receiver operating characteristic curve of each model



AUC:0.813 (95%CI:0.727-0.881) AUC:0.768 (95%CI:0.677-0.843) AUC:0.787 (95%CI:0.698-0.860)

Results

Patients characteristics are shown in Table 2, and outcomes at 6 months after injury are shown in Table 3. Seventy-seven percent of 109 patients had an unfavorable outcome, and 23% had a favorable outcome.

Receiver operating characteristic (ROC) curve is shown in Figure 1. The area under the ROC curve (AUC) for our model was 0.813 (95% CI of 0.727-0.881), and higher than the other two models, although there was no significant difference among the models.

Figure 2 shows the probability of an unfavorable outcome of each predictive model plotted in unfavorable and favorable outcome at 6 months after injury. Friedman test was performed to compare the predictive value in three models. In unfavorable outcome group, predictive value of our model was higher than that of IMPACT or CRASH models. In favorable outcome, those of our model and CRASH were higher than IMPACT, but there was no significant difference between our model and CRASH.

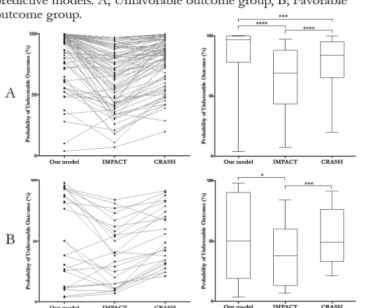
When the cut-off value was determined according to Youden Index, it was imposed at 0.960 in our model, 0.420 in IMPACT, 0.720 in CRASH respectively (Figure 3).

In our model, positive predictive value and specificity were higher than the other models, but negative predictive value and sensitivity were lower compered to the two models (Table 4).

Table 3. Glasgow Outcome Scale in 109 patients 6 months after severe traumatic brain injury

Glasgow Outcome Scale	n (%)
Good recovery	10 (9.2)
Moderate disability	15 (13.8)
Severe disability	27 (24.8)
Persistent vegetative state	12 (11.0)
Death	45 (41.3)

Figure 2. The probability of unfavorable outcome plotted on three predictive models. A; Unfavorable outcome group, B; Favorable outcome group.



(*p<0.05, **p<0.001, ***p<0.0001)

Figure 3. The probability of an unfavorable outcome plotted against the actual outcome. Each red solid line indicates cut-off value.

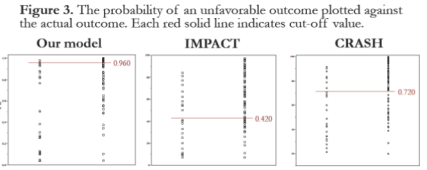


Table 4. Comparison of prediction accuracy with three prediction models

	Our model	IMPACT	CRASH
Positive predictive value (%)	97.8	87.0	88.4
Negative predictive value (%)	37.5	46.9	43.9
Sensitivity (%)	52.4	79.8	72.6
Specificity (%)	96.0	60.0	72.0

Conclusion

Our prognostic model was shown to have high predictive value on external validation, and was equivalent to IMPACT or CRASH models in predictive accuracy.

Conflict of interest

None

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