



Prognostic Predictors of Early Outcomes and Discharge Status of Patients Undergoing Decompressive Craniectomy After Severe Traumatic Brain Injury

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■ **OBJECTIVE:** Although several prognostic factors for traumatic brain injury (TBI) have been evaluated, a useful predictive scoring model for the outcomes has not been developed for patients with severe TBI who undergo decompressive craniectomy (DC). The aim of the present study was to determine independent predictors and develop a multivariate logistic regression equation to predict the early outcome and discharge status for patients with severe TBI who have undergone DC.

■ **METHODS:** A total of 13 different variables were evaluated. The data from all 278 patients with severe TBI who had undergone DC in the present study were retrospectively evaluated from July 2011 to June 2017. Using univariate, multiple logistic regression and prognostic regression scoring equations it was possible to draw receiver operating characteristic curves to predict the early outcomes and discharge status after TBI.

■ **RESULTS:** We found that younger age ($P = 0.012$), no significant medical history ($P = 0.044$), diameter of both pupils <4 mm ($P = 0.032$), higher admission Glasgow coma scale score ($P = 0.004$), no tracheotomy ($P < 0.001$), and DC for severe TBI were associated with a favorable early outcome and discharge status. Using receiver operating characteristic curves to predict the probability of a favorable outcome, the sensitivity was 80.0% and the specificity was 79.5%.

■ **CONCLUSIONS:** Our preliminary findings have shown that 5 variables can be used as independent predictors in assessing the early outcome and discharge status for patients with severe TBI after DC.

INTRODUCTION

Traumatic brain injury (TBI) poses a critical public health problem and constitutes a major cause of death and severe disability among young people.¹ Decompressive craniectomy (DC) involves removing a component of the bony skull to allow for cerebral tissue expansion to reduce intracranial pressure (ICP). Although the DECRA trial (early decompressive craniectomy in patients with severe traumatic brain injury) showed that neuroprotective bifrontal DC for moderate intracranial hypertension is not helpful, the RESCUEicp (Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of Intracranial Pressure) trial found that last-tier DC for severe and refractory intracranial hypertension can significantly reduce the mortality rate, although it was associated with a greater rate of disability.^{2,3} The conclusions from the DECRA trial raised several criticisms, and DC for patients with severe TBI remains a highly debated issue. In addition, considerable research has shown that DC is an effective method for controlling high ICP and improving functional outcome and mortality, especially for patients with severe TBI.^{4,5} As a reliable life-saving treatment, DC is still frequently performed; hence, the

Key words

- Decompressive craniectomy
- Discharge status
- Prognostic predictors
- Severe traumatic brain injury

Abbreviations and Acronyms

- CI:** Confidence interval
- CT:** Computed tomography
- DC:** Decompressive craniectomy
- GCS:** Glasgow coma scale
- GOS:** Glasgow Outcome Score
- ICP:** Intracranial pressure
- OR:** Odds ratio
- ROC:** Receiver operating characteristic
- TBI:** Traumatic brain injury

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Citation: World Neurosurg. (2019) 126:e101-e108.
<https://doi.org/10.1016/j.wneu.2019.01.246>

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

1878-8750/\$ - see front matter © 2019 Published by Elsevier Inc.

prediction of postoperative outcomes is highly important and imperative in neurosurgical practice. Previous research has shown the predictors of favorable outcomes for all patients with TBI included younger age, higher Glasgow coma scale (GCS) scores on admission, and the lack of associated lesions signifying damage to the underlying cortex, such as contusions or intraparenchymal hemorrhage.^{6,7} However, a useful outcome predictive scoring model or multivariate logistic regression equation has not been well established for patients with severe TBI undergoing DC.

Thus, the aim of the present study was to determine the independent prognostic factors and develop a multivariate logistic regression equation to delineate those patients who might have more favorable outcomes after DC to treat severe TBI. Specifically, we assessed the pre- and postoperative factors associated with the short-term outcomes, including discharge status as a primary predefined outcome.

METHODS

Patients

Patients presenting to our center with TBI, including mild, moderate, and severe head injury, during the 6-year study period from July 2011 to June 2017, who had undergone DC were identified. The records of these patients were extracted retrospectively from the hospital's computerized electronic database. We retrospectively collected data for those patients with a history of severe TBI and an admission GCS score of 3–8. The exclusion criteria were any previous disabled neurological disease, previous craniectomy, spinal cord injury, penetrating head injury, and alcohol intoxication. The ethical committee of Beijing Tian Tan Hospital, Capital Medical University, approved the present study.

Decompressive Craniectomy

The key indications for DC were as follows: thickness >1 cm in the case of extracerebral hematoma and a volume >30 mL in the case of intracerebral hematoma, deviation of the supratentorial midline shift >5 mm with lateral ventricle compression, disappearance of the basal cistern, and ongoing clinical symptoms that had worsened since the injury had occurred. When the patients required DC, a standardized surgical approach, which had been modeled on the technique reported by Liu et al.,⁸ was used. This approach included a unilateral craniectomy or bilateral craniectomy opening to maximize the reduction in ICP. The type of craniectomy performed (unilateral vs. bilateral) was determined from the computed tomography (CT) findings. Unilateral craniectomy was performed in patients with unilateral swelling; however, for patients with general swelling, we performed bilateral craniectomy.⁹ The area covered by the unilateral craniectomy was ~12 cm × 15 cm and by the bilateral craniectomy was ~10 cm × 25 cm.⁸

Variables

The relationship of patient age, sex, injury mechanism, medical history, concurrent injury, dilated pupils, pupillary reactivity, admission GCS score, Marshall CT grade, tracheotomy, interval from injury to surgery, operative style (unilateral or bilateral DC), length of stay in the hospital, and Glasgow outcome scale (GOS) score at discharge were evaluated. For the convenience of the data

analysis, the presence of a dilated pupil was defined as a pupil diameter >4 mm. The dilated pupil was divided into 3 categories: 1 pupil dilated, both pupils dilated, and neither pupil dilated. Pupillary light reactivity was also divided into 3 categories: brisk, sluggish, and nonreactive. We used the Marshall CT grade to evaluate the midline shift on the CT scan. The interval between TBI and surgery was classified as very early surgery (<6 hours after injury), early surgery (6–24 hours), and late surgery (>24 hours). The outcome of patients at discharge was categorized using the GOS score as follows: score 1, death; score 2, persistent vegetative state; score 3, severe disability (conscious but disabled); score 4, moderate disability (disabled but independent); and score 5, good recovery. A score of 4–5 was considered a favorable outcome (moderate disability or less), and a score of 1–3 was considered an unfavorable outcome (severe disability or death).¹⁰

Statistical Analysis

Data are presented as the mean ± standard deviation or numbers and percentages. Student t tests or χ^2 tests were used to assess the statistical significance among all groups. Multiple logistic regression models were used for correlation between 2 continuous or categorical variables, and the independent risk factors for poor outcome were defined. Finally, logistic regression analysis was then used to establish a prognostic model, and a receiver operating characteristic (ROC) curve was drawn according to the prognostic scoring model.¹¹ All data were analyzed using statistical software SPSS, version 18 (IBM Corp., Armonk, New York, USA). A P value < 0.05 was considered to indicate statistical significance.

RESULTS

From July 2011 to June 2017, a total of 3628 patients who had been admitted to our departments and treated for mild, moderate, or severe TBI were identified. Of these 3628 patients, 278 patients with severe TBI who had undergone DC were identified. Their data were retrospectively collected and evaluated for the present study. The patient data and clinical characteristics are summarized in **Table 1**. The mean age of the 278 patients was 49.3 ± 15.5 years (range, 15–86), and the percentage of male patients was 79.9%. Traffic accidents had occurred in more than one half of all cases (53.6%). The common concurrent injury was bone fracture, and most of the patients with TBI (78.4%) had undergone DC within 24 hours after injury. The overall mortality at discharge was 37.1% (103 of 278). Of the 278 patients, 102 (36.7%) had been discharged in a persistent vegetative state or with severe disability and 73 had been discharged with a favorable outcome (26.3%).

Age ($P < 0.001$), admission GCS score ($P < 0.001$), and hospital length of stay ($P = 0.008$) were significantly associated with the discharge GOS score after injury using Student t test analysis for continuous variables (**Table 2**). The results of the χ^2 or Fisher exact test for categorical variables showed that medical history ($P = 0.002$), dilated pupil ($P < 0.001$), pupillary reactivity ($P < 0.001$), and tracheotomy ($P < 0.001$) were significantly associated with the discharge GOS score after injury (**Table 3**). Multivariate logistic regression was performed of the significant variables extracted from the previous step to determine the independent associations of each variable with the discharge GOS score after injury. These results showed that age (odds

Table 1. Patient Demographic and Clinical Data

Characteristic	Mean ± SD or n (%)
Age (years)	49.3 ± 15.5
Sex	
Female	56 (20.1)
Male	222 (79.9)
Injury mechanism	
Fall	106 (38.1)
Traffic accident	149 (53.6)
Attack	23 (8.3)
Medical history	
Healthy	122 (43.9)
Hypertension	61 (22.0)
Diabetes	24 (8.6)
Heart disease	18 (6.5)
Oral aspirin use	19 (6.8)
Other	34 (12.2)
Concurrent injury	
None	191 (68.7)
Bone fracture	72 (25.9)
Lung contusion	10 (3.6)
Other	5 (1.8)
Dilated pupil	
Diameter of both pupils <4 mm	130 (46.8)
Diameter of 1 pupil ≥4 mm	104 (37.4)
Diameter of both pupils ≥4 mm	44 (15.8)
Pupillary reactivity	
Brisk	31 (11.2)
Sluggish	77 (27.7)
Nonreactive	170 (61.2)
Admission GCS score	5.14 ± 1.55
3	59 (21.2)
4	28 (10.1)
5	86 (30.9)
6	54 (19.4)
7	21 (7.6)
8	30 (10.8)
Marshall CT grade	4.41 ± 1.44
II	25 (9.0)
III	66 (23.7)
IV	70 (25.2)
Continues	

Table 1. Continued

Characteristic	Mean ± SD or n (%)
V	3 (1.1)
VI	114 (41.0)
Tracheotomy	
Yes	105 (37.8)
No	173 (62.2)
Interval from injury to surgery (hours)	
≤6	113 (40.6)
6–24	105 (37.8)
>24	60 (21.6)
Operation style	
Unilateral DC	237 (85.3)
Bilateral DC	41 (14.7)
Mortality at discharge	103 (37.1)
Discharge GOS score	2.49 ± 1.44
Unfavorable outcome (GOS score 1–3)	205 (73.7)
Favorable outcome (GOS score 4–5)	73 (26.3)
Hospital length of stay (days)	16.8 ± 13.8
SD, standard deviation; GCS, Glasgow coma scale; CT, computed tomography; DC, decompressive craniectomy; GOS, Glasgow outcome scale.	

ratio [OR], 0.971; 95% confidence interval [CI], 0.949–0.993; $P = 0.012$), medical history (OR, 0.840; 95% CI, 0.709–0.995; $P = 0.044$), dilated pupil (OR, 0.531; 95% CI, 0.297–0.946; $P = 0.032$), admission GCS score (OR, 2.984; 95% CI, 1.419–6.272; $P = 0.004$), and tracheotomy (OR, 0.139; 95% CI, 0.058–0.332; $P < 0.001$) were independently associated with the discharge GOS score (Table 4). We found that younger age, no significant medical history, diameter of both pupils <4 mm, higher admission GCS score, no tracheotomy, and DC for severe

Table 2. Relationship of Continuous Variables to Discharge Outcome Postoperatively After Univariate Analysis

Variable	Favorable Outcome (n = 73)	Unfavorable Outcome (n = 205)	P Value*
Age (years)	43.2 ± 14.1	51.5 ± 15.4	<0.001†
Admission GCS score	6.07 ± 1.37	4.81 ± 1.48	<0.001†
Marshall CT grade	4.38 ± 1.50	4.42 ± 1.43	0.835
Hospital length of stay (days)	20.67 ± 10.70	15.44 ± 14.56	0.008†
GCS = Glasgow coma scale; CT, computed tomography. *Student <i>t</i> test. †Statistically significant.			

Table 3. Relationship of Categorical Variables to Discharge Outcome Postoperatively After univariate Analysis

Variable	Favorable Outcome	Unfavorable Outcome	P Value*
Sex			0.563
Female	13 (23.2)	43 (76.8)	
Male	60 (27.0)	162 (73.0)	
Injury mechanism			0.624
Fall	32 (30.2)	74 (69.8)	
Traffic accident	33 (22.1)	116 (77.9)	
Attack	8 (34.8)	15 (65.2)	
Medical history			0.002†
Healthy	39 (32.0)	83 (68.0)	
Hypertension	12 (19.7)	49 (80.3)	
Diabetes	1 (4.2)	23 (95.8)	
Heart disease	1 (5.6)	17 (94.4)	
Oral aspirin use	1 (5.3)	18 (94.7)	
Other	19 (55.9)	15 (44.1)	
Concurrent injury			0.201
None	52 (27.2)	139 (72.8)	
Bone fracture	20 (27.8)	52 (72.2)	
Lung contusion	1 (10.0)	9 (90.0)	
Other	0 (0)	5 (100)	
Dilated pupil			<0.001†
Diameter of both pupils <4 mm	48 (36.9)	82 (63.1)	
Diameter of 1 pupil ≥4 mm	22 (21.2)	82 (78.8)	
Diameter of both pupils ≥4 mm	3 (6.8)	41 (93.2)	
Pupillary reactivity			<0.001†
Brisk	12 (38.7)	19 (61.3)	
Sluggish	32 (41.6)	45 (58.4)	
Nonreactive	29 (17.1)	141 (82.9)	
Tracheotomy			<0.001†
Yes	7 (6.7)	98 (93.3)	
No	66 (38.2)	107 (61.8)	
Interval from injury to surgery (hours)			0.876
≤6	29 (25.7)	84 (74.3)	
6–24	26 (24.8)	79 (75.2)	
>24	18 (30)	42 (70)	

Continues

Table 3. Continued

Variable	Favorable Outcome	Unfavorable Outcome	P Value*
Operation style			0.073
Unilateral DC	67 (28.3)	170 (71.7)	
Bilateral DC	6 (14.6)	35 (85.4)	

DC, decompressive craniectomy.
* χ^2 test.
†Statistically significant.

TBI were associated with a favorable early outcome and discharge status.

A predicted probability (P) of a favorable outcome was estimated using the multiple logistic regression model: $\text{Ln}(P/1 - P) = 1.879 - 0.029 \times (\text{age in years}) - 0.167 \times (\text{medical history}) - 0.601 \times (\text{dilated pupil}) + 0.430 \times (\text{admission GCS score}) - 1.973 \times (\text{tracheotomy})$. The predictors of the model were selected using a stepwise procedure. Using ROC curve analysis based on the prognostic model scoring, a cutoff point for the prediction of a favorable outcome of P was defined as 2.21. The sensitivity of the equation was 80.0% and the specificity was 79.5% for predicting favorable early outcomes at discharge after TBI (area under the curve, 0.835; 95% CI, 0.783–0.887; **Figure 1**).

We also performed further subgroup analysis for the independently associated variables. For the 278 patients with severe TBI who had undergone DC in our cohort, the percentage of good outcomes for patients aged ≤65 years was 29.0% (71 of 245). In contrast, the percentage of poor outcomes for patients aged >65 years was 93.9% (31 of 33; OR, 0.158; 95% CI, 0.037–0.678; $P = 0.013$). Thus, 65 years of age could be used as a key cutoff point for predicting outcomes after DC, which was consistent with the findings from other related studies. In the subgroup analysis

Table 4. Final Model of Multiple Logistic Regression Constructed Using Forward Stepwise Procedure and Adjusted Odds Ratio for Predicting Glasgow Outcome Scale Score 4–5 versus 1–3

Variable	β	OR	95% CI	P Value
Age	−0.029	0.971	0.949–0.993	0.012*
Medical history	−0.167	0.840	0.709–0.995	0.044*
Dilated pupil	−0.601	0.531	0.297–0.946	0.032*
Admission GCS score	0.430	2.984	1.419–6.272	0.004*
Tracheotomy	−1.973	0.139	0.058–0.332	<0.001*
Constant	1.879			

β , interception of coefficient; OR, odds ratio; CI, confidence interval; GCS, Glasgow coma scale.
*Statistically significant.

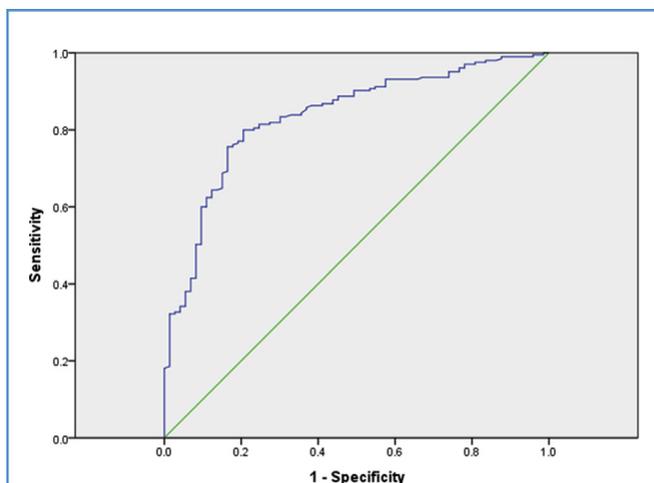


Figure 1. Receiver operating characteristic curve drawn based on data from the prognostic scoring model: $\text{logistic} = \text{Ln}(P/1 - P) = 1.879 - 0.029 \times (\text{age in years}) - 0.167 \times (\text{medical history}) - 0.601 \times (\text{dilated pupil}) + 0.430 \times (\text{admission Glasgow coma scale score}) - 1.973 \times (\text{tracheotomy})$, where medical history and health = 0, hypertension, diabetes, heart disease, oral aspirin use = 1; dilated pupil, diameter of both pupils <4 mm = 0, diameter of ≥ 1 pupil ≥ 4 mm = 1; tracheotomy, no = 0, and tracheotomy, yes = 1.

of 245 patients aged <65 years, the percentage of good outcomes for those aged <55 years was 32.7% (56 of 171). In contrast, the percentage of poor outcomes was 79.7% (59 of 74) for those aged 55–65 years (OR, 0.498; 95% CI, 0.264–0.937; $P = 0.031$). This finding implies that 55 years of age might also be a key cutoff point for predicting the outcomes after surgery. In the subgroup analysis of medical history factors, our data showed that a medical history of hypertension (OR, 0.696; 95% CI, 0.487–0.995; $P = 0.047$), diabetes (OR, 0.293; 95% CI, 0.106–0.810; $P = 0.018$), heart disease (OR, 0.341; 95% CI, 0.123–0.949; $P = 0.039$), and oral aspirin use (OR, 0.332; 95% CI, 0.120–0.920; $P = 0.034$) were the factors associated with unfavorable discharge outcomes. In addition, compared with patients with a diameter of both pupils of ≥ 4 mm (44 of 278), patients with a diameter of both pupils of <4 mm (130 of 278; OR, 0.354; 95% CI, 0.192–0.652; $P = 0.001$) or only 1 pupil diameter of ≥ 4 mm (104 of 278; OR, 0.273; 95% CI, 0.077–0.965; $P = 0.044$) experienced better discharge outcomes. Also, patients with a diameter of both pupils <4 mm also experienced much better discharge outcomes compared with those with 1 pupil diameter of ≥ 4 mm (OR, 0.458; 95% CI, 0.254–0.827; $P = 0.010$). The vast majority of DC was performed within the first 24 hours (218 of 278; 78.4%) after TBI, which could be considered as DC for primary TBI. The remaining 21.6% (60 of 278) could be considered as DC for secondary refractory ICP elevations. The subset analysis comparing the outcomes between these 2 varied groups showed no statistically significant differences ($P = 0.458$).

DISCUSSION

DC reduces medically refractory intracranial hypertension and is a valuable tool in the management of head injury. DC has been

historically considered a salvage procedure for patients with severe TBI.^{12,13} However, the prognosis of patients after DC has varied highly. Skoglund et al.¹⁴ reported that 68% of patients with TBI had favorable outcomes,¹⁴ and Jiang et al.¹⁵ and Ucar et al.¹⁶ indicated that 60.2% and 84% of patients, respectively, experienced unfavorable outcomes after DC. In clinical practice, quantitative prognostic estimates have been of particular importance to the heterogeneous condition of TBI and could be applied to clinical decision-making and assessment of the need for long-term care. Lingsma et al.¹⁷ reported that age, clinical severity of intracranial injuries (GCS score), CT abnormalities, systemic insults (hypoxia and hypotension), and laboratory variables are relevant predictive factors for the outcomes of patients with moderate and severe TBI. The CRASH (corticosteroid randomization after significant head injury) study and IMPACT (international mission for prognosis and analysis of clinical trials in traumatic brain injury) are 2 important prognostic models for patients with moderate and severe TBI. Both perform quite well even early after injury. The CRASH study included 10,008 cases mainly from developing countries; therefore, the CRASH prognostic model is mainly suitable for developing countries. IMPACT included 9205 patients mainly from developed countries and, thus, is more suitable for developed countries. Numerous differences, including the targets and requirements for treatment of severe TBI, have been noted between developing and developed countries. However, given the lack of balance in state development in China with both developing and developed characteristics, the establishment of a mixed characteristics prognostic model for severe TBI after DC treatment would also be beneficial. This was one of the reasons we constructed our prognostic model for patients with severe TBI after DC. We found that the overall mortality rate and unfavorable outcome rate for patients with severe TBI who had undergone DC was 37.1% and 73.7%, respectively, consistent with the results reported by Kuo et al.¹⁸ We also found that younger age, no significant medical history, diameter of both pupils <4 mm, higher admission GCS score, no tracheotomy, and DC for severe TBI were factors associated with favorable early outcomes and discharge status.

The direct relationship between increasing age and poor post-traumatic outcome after surgical intervention in patients with TBI has been well reported.^{12,19–21} Ono et al.²² demonstrated that for patients aged <40 years, the percentage of good outcomes ranged from 33.9% to 48.7% for different lesions. In contrast, the incidence of poor outcomes ranged from 66.7% to 94.4% in patients aged >40 years. In a retrospective cohort of 55 patients with severe head injury, Pompucci et al.²³ showed that age >65 years and a poor GCS score of 3–5 at presentation were adversely associated with functional outcomes in patients with TBI who had undergone DC. Our results revealed that age was an independent predictor of the early outcome and discharge status in patients with severe TBI undergoing DC, and younger patients had better early outcomes after operative intervention, consistent with the findings from previous reports. In the present study, after univariate analysis, the results showed an age of 43.2 ± 14.1 years for favorable outcomes and 51.5 ± 15.4 years for unfavorable outcomes ($P < 0.001$). Using multiple logistic regression models, the adjusted OR for the prediction of

poor outcomes was significant with age (OR, 0.971; 95% CI, 0.949–0.993; $P = 0.012$). Similar to the findings from previous studies,^{23,24} we found that 65 years of age could be used as a key cutoff point for predicting the outcome after surgery. The percentage of good outcomes for patients aged <65 years was 29.0% (71 of 245), and the percentage of poor outcomes was 93.9% (31 of 33) for those aged >65 years among the 278 patients with severe TBI who had undergone DC in our cohort (OR, 0.158; 95% CI, 0.037–0.678; $P = 0.013$). It is undeniable that older people were much more likely to have a variety of age-related diseases compared with younger individuals, and the physical function of the elderly were occasionally too poor to cope with the TBI. For example, 14 of the 33 older patients (42.4%) had hypertension and 10 (30.3%) took oral aspirin. In contrast, among the 245 patients aged <65 years, only 50 (20.4%) had hypertension and 9 (3.7%) were taking oral aspirin. These results have demonstrated that the age-related diseases common to patients aged >65 years could have potentially influenced their poor outcomes after TBI. We also performed further exploratory subgroup analysis of the 245 patients aged <65 years and found that the percentage of good outcomes for those aged <55 years of age was 32.7% (56 of 171), and poor outcomes were noted in 79.7% (59 of 74) of patients aged 55–65 years (OR, 0.498; 95% CI, 0.264–0.937; $P = 0.031$). These results implied that 55 years of age might serve as a key cutoff point for predicting the outcomes after surgery. Establishing a better correlation between patient age and outcomes is important for predicting the outcome and understanding how to adjust for age in epidemiological studies. Furthermore, identifying threshold values might be relevant to clinical research and clinical practice (i.e., for purposes of stratification in randomized clinical trials or prognostic modeling). Also, more detailed age stratification might lead to more accurate results. Increasing age has been associated with a poorer outcome for patients with systemic diseases, such as cancer, coronary heart disease, and neurological disease, such as subarachnoid hemorrhage and dementia. In a large meta-analysis of 5600 patients, Hukkelhoven et al.⁷ found that the association between patient age and outcome after severe TBI was a continuous function, which could be adequately described using an age linear term. These results supported the hypothesis that the adult brain exhibits a decreased capacity for repair as it ages.²⁵ The brain's increased exposure to minor repetitive (often subclinical) insults as age increases and the presence of systemic comorbidities (e.g., vasculopathy, neuropathy) are also most likely contributors to the brain's reduced capacity for repair.

Pupil reactivity to light stimulus has been correlated with outcome by several studies. A bilateral absent pupillary light reflex was associated with mortality of 56%–90%.²⁶ Kuo et al.²⁷ demonstrated that pupil reactivity to light had the most significant correlation with the GOS score ($P = 0.727$ and $P < 0.0001$, respectively) compared with coagulopathy and midline shift. It has been reported that most patients classified as having both pupils fixed would have a very poor outcome,²⁷ and some studies have concluded that patients with an initial GCS score of 3 and bilateral pupillary size of ≥ 4 mm will have no chance of recovery or will experience 100% in-hospital mortality.^{28,29} However, Carter et al.³⁰ reported that ~20% of patients with a bilaterally absent pupillary response had favorable outcomes in a study of 89 patients. The present study revealed

that the percentage of patients with an unfavorable outcome was 63.1% when the diameter of both pupils was <4 mm, 78.8% if 1 pupil diameter was ≥ 4 mm, and 93.2% if the diameter of both pupils was ≥ 4 mm ($P < 0.001$). The adjusted ORs for a diameter of both pupils <4 mm versus ≥ 1 pupil diameter of ≥ 4 mm are presented in Table 4 (OR, 0.531; 95% CI, 0.297–0.946; $P = 0.032$). These results were consistent with those from some previous reports. In subgroup analysis, however, only 20% (41 of 205) of the unfavorable outcomes occurred in patients with a diameter of both pupils of ≥ 4 mm. In addition, 3 of 44 patients (6.8%; 2 patients with a discharge GOS score of 5 and 1 with a discharge GOS score of 4) with a diameter of both pupils of ≥ 4 mm experienced a favorable discharge outcome after life-saving DC after severe TBI. In addition, 11 of 44 patients (25%; 3 patients with a discharge GOS score of 3 and 8 with a discharge GOS score of 2) with a diameter of both pupils of ≥ 4 mm had an unfavorable discharge but a positive survival outcome in our cohort. All these patients were sent to other rehabilitation hospitals for subsequent treatment. The improved cerebral blood flow and metabolism caused by the reduction of ICP after DC might have been one of the major reasons for the favorable outcomes, and patients might have benefited much more from DC than we had expected. Thus, from our research data and humanitarian considerations, especially for those patients whose family members strongly requested surgery, we would recommend that patients with a diameter of both pupils of ≥ 4 mm should also be actively undergoing life-saving DC as soon as possible after severe TBI.

In addition to the single-factor analysis and multifactorial prognostic analysis, we combined an ROC curve and multivariate logistic regression equation to evaluate the predictive accuracy of 5 variables with the GOS score. Our results revealed that all 5 variables, which had previously been shown to be related to survival, exhibited appropriate accuracy in prognostic judgment, with 80.0% sensitivity and 79.5% specificity for the discharge outcome. We also chose the CRASH prediction model, which defined the outcome as mortality at 14 days, to compare with our prognostic model. The observed outcomes in our cohort population revealed a 14-day mortality of 32.7% with a 73.7% unfavorable outcome rate. The CRASH-based model predicted the 14-day mortality to be 30.2%, and our prognostic model predicted for a 70.6% rate of unfavorable early outcome and discharge status. Both the CRASH model and our prognostic model performed well with an area under the curve of 0.852 and 0.835, respectively, showing that our prognostic model also had good discrimination and calibration similar to the CRASH model. Because these 5 variables in the scoring model are clinically simple to attain in the acute setting after TBI, we consider that the derived equation will be clinically useful for predicting the outcome in daily practice.

One limitation of the present study was related to its single-center, nonrandomized, retrospective study design, which was susceptible to selection and information bias. This was an institutional study, and many surgeons (with variable experience) treated these patients. The data regarding postoperative ICP monitoring were also insufficient, given the economic burden and lack of comprehensive monitoring in previous clinical work. Thus, we could not analyze the important ICP factors associated with outcomes, a significant confounding factor. Additional limitations

of the present study include the small sample size and heterogeneity of the patient population. The different types of TBI, such as epidural hematoma, subdural hematoma, and contusion hemorrhage, will result in different outcomes. However, in our study, the outcome predictors, such as age, medical history, dilated pupil, pupillary reactivity, admission GCS score, tracheotomy, operation style, and hospital length of stay, are all important factors for any type of brain insult. In general, it seemed reasonable to group these patients together, and subgroup analysis of an enriched population of patients with different types of hemorrhage is needed to clarify the issue in future research. In addition, pupil reactivity and pupil diameter in our cohort were examined using a medical flashlight and ruler by experienced neurosurgeons. However, pupillometry, which is more convenient and accurate for measuring the pupils, has been of great importance and had prognostic value for patients with TBI. This method could add value to patient care and critical decision-making, as previous studies have reported, and the use of pupillometry as a bedside tool in the routine care of patients with TBI should be widespread and promoted in future clinical work and research. Finally, our work examined only the short-term outcomes, which were defined by the location to which the patients were discharged, and did not address the long-term outcomes or the quality of life the patients

could expect in what will often be a long process to recovery. Thus, future studies should focus on the long-term functional outcomes.

CONCLUSIONS

Our findings have revealed that 5 factors, including younger age, no significant medical history, no dilated pupils, higher admission GCS score, and no tracheotomy during treatment, were associated with favorable outcomes for patients with severe TBI. These factors can be used as independent predictors in assessing the early outcome and discharge status for patients with severe TBI after DC treatment. The 5 variables identified from our multivariate logistic equation will also be clinically useful for predicting the outcomes in daily practice.

ACKNOWLEDGMENTS

We express our sorrow to the patients involved in the present study. These data are not just simple numbers but disasters for entire families, and we wish such tragedies would never happen. In addition, we would like to acknowledge the assistance of Fei Gao and Mengshi Yang for their support of our study.

REFERENCES

- Alarcon JD, Rubiano AM, Okonkwo DO, Urrutia G, Cosp XB. Elevation of the head during intensive care management in patients with severe traumatic brain injury. *Cochrane Database Syst Rev*. 2017;12:CD00986.
- Cooper DJ, Rosenfeld JV, Murray L, et al. The DECRA trial investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group. *N Engl J Med*. 2011;364:1493-1502.
- Hutchinson PJ, Koliak AG, Timofeev IS, et al. Trial of decompressive craniectomy for traumatic intracranial hypertension. *N Engl J Med*. 2016;375:1119-1130.
- Galgano M, Toshkezi G, Qiu X, Russell T, Chin L, Zhao LR. Traumatic brain injury: current treatment strategies and future endeavors. *Cell Transplant*. 2017;26:1118-1130.
- Shutter LA, Timmons SD. Intracranial pressure rescued by decompressive surgery after traumatic brain injury. *N Engl J Med*. 2016;375:1183.
- Lemcke J, Alzain F, von der Brölie C, Ebenau M, Meier U. The influence of coagulopathy on outcome after traumatic subdural hematoma: a retrospective single-center analysis of 319 patients. *Blood Coagul Fibrinolysis*. 2014;25:353-359.
- Hukkelhoven CW, Steyerberg EW, Rampen AJ, et al. Patient age and outcome following severe traumatic brain injury: an analysis of 5600 patients. *J Neurosurg*. 2003;99:666-673.
- Liu B, Jiang J, Zhang S. The introduction of decompressive craniectomy for traumatic brain injury patients. *Chinese J Neurosurg*. 2008;24:153-154.
- Mao X, Miao G, Hao S, et al. Decompressive craniectomy for severe traumatic brain injury patients with fixed dilated pupils. *Ther Clin Risk Manag*. 2015;11:1627-1633.
- Teasdale GM, Pettigrew LE, Wilson JT, Murray G, Jennett B. Analyzing outcome of treatment of severe head injury: a review and update on advancing the use of the Glasgow outcome scale. *J Neurotrauma*. 1998;15:587-597.
- Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem*. 1993;39:561-577.
- Barthélemy EJ, Melis M, Gordon E, Ullman JS, Germano I. Decompressive craniectomy for severe traumatic brain injury: a systematic review. *World Neurosurg*. 2016;88:411-420.
- Honeybul S, Ho KM. Predicting long-term neurological outcomes after severe traumatic brain injury requiring decompressive craniectomy: a comparison of the CRASH and IMPACT prognostic models. *Inj J Care Inj*. 2016;47:1886-1892.
- Skoglund TS, Erikssonritzen C, Jensen C, Rydenhag B. Aspects on decompressive craniectomy in patients with traumatic head injuries. *J Neurotrauma*. 2006;23:1502-1509.
- Jiang JY, Xu W, Li WP, et al. Efficacy of standard trauma craniectomy for refractory intracranial hypertension with severe traumatic brain injury: a multicenter, prospective, randomized controlled study. *J Neurotrauma*. 2005;22:623-628.
- Ucar T, Akyuz M, Kazan S, Tuncer R. Role of decompressive surgery in the management of severe head injuries: prognostic factors and patient selection. *J Neurotrauma*. 2005;22:1311-1318.
- Lingsma HF, Roozenbeek B, Steyerberg EW, Murray GD, Maas AI. Early prognosis in traumatic brain injury: from prophecies to predictions. *Lancet Neurol*. 2010;9:543-554.
- Kuo JR, Yeh TC, Sung KC, Wang CC, Chen CW, Chio CC. Intraoperative applications of intracranial pressure monitoring in patients with severe head injury. *J Clin Neurosci*. 2006;13:218-223.
- Fotakopoulos G, Tsianaka E, Vagkopoulos K, Fountas KN. According to which factors in severe traumatic brain injury craniectomy could be beneficial. *Surg Neurol Int*. 2016;7:19.
- Zador Z, Sperrin M, King AT. Predictors of outcome in traumatic brain injury: new insight using receiver operating curve indices and Bayesian network analysis. *PLoS One*. 2016;11:e0158762.
- Mosenthal AC, Livingston DH, Lavery RF, et al. The effect of age on functional outcome in mild traumatic brain injury: 6-month report of a prospective multicenter trial. *J Trauma Acute Care Surg*. 2004;56:1042-1048.
- Ono J, Yamaura A, Kubota M, Okimura Y, Isobe K. Outcome prediction in severe head injury: analyses of clinical prognostic factors. *J Clin Neurosci*. 2001;8:120-123.
- Pompucci A, De Bonis P, Pettorini B, Petrella G, Di Chirico A, Anile C. Decompressive craniectomy for traumatic brain injury: patient age and outcome. *J Neurotrauma*. 2007;24:1182-1188.
- De Bonis P, Pompucci A, Mangiola A, et al. Decompressive craniectomy for elderly patients with traumatic brain injury: it's probably not worth the while. *J Neurotrauma*. 2011;28:2043-2048.

25. Carlsson CA, von Essen C, Löfgren J. Factors affecting the clinical course of patients with severe head injuries. *J Neurosurg.* 1968;29:242.
26. Fountain DM, Kolas AG, Lecky FE, et al. Survival trends after surgery for acute subdural hematoma in adults over a 20-year period. *Ann Surg.* 2017;265:590-596.
27. Kuo JR, Chou TJ, Chio CC. Coagulopathy as a parameter to predict the outcome in head injury patients—analysis of 61 cases. *J Clin Neurosci.* 2004;11:710-714.
28. Hoffmann M, Lefering R, Rueger JM, et al. Pupil evaluation in addition to Glasgow coma scale components in prediction of traumatic brain injury and mortality. *Br J Surg.* 2011;99(suppl 1):122-130.
29. Leitgeb J, Mauritz W, Brazinova A, et al. Glasgow coma scale score at intensive care unit discharge predicts the 1-year outcome of patients with severe traumatic brain injury. *Eur J Trauma Emerg Surg.* 2013;39:285-292.
30. Carter B, Butt AW. Bilaterally absent pupillary responses: not always a bad sign. *Anaesth Intensive Care.* 2007;35:984-987.

Conflict of interest statement: The present study was supported by the National Natural Science Foundation of

China (grants 81801225, 81171144, and 81471238), Natural Science Foundation of Capital Medical University (grant PYZ2017075), and Youth Foundation of Beijing Tian Tan Hospital (grant 2017-YQN-03).

Received 26 September 2018; accepted 24 January 2019

Citation: World Neurosurg. (2019) 126:e101-e108.

<https://doi.org/10.1016/j.wneu.2019.01.246>

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

1878-8750/\$ - see front matter © 2019 Published by Elsevier Inc.