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Simple Prognostic Scale for Traumatic Brain Injury Patients without Neurosurgical Treatment

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Abstract

Objective: Traumatic brain injury (TBI) is a major global public health issue and thus searching for new prognostic tools can be useful in creating an optimal strategy for the management of patients after TBI. We aimed to develop and validate a simple prognostic scale using admission characteristics to predict functioning outcome at 6-months post admission in patients with different degrees of brain injury without immediate neurosurgical intervention.

Methods: We created the simple prognostic scale based on the medical admission data from 184 neurology department patients after TBI and 6-months outcome according to the Glasgow Outcome Scale (GOS). All potential predictors with the significance level of $p<0.05$, identified in a univariate analysis, were included in the multivariate models. A multivariate logistic regression analysis was carried out using backward elimination to identify independent predictors ($p<0.05$). The relative weighting of each individual component of the scale was determined from the relative change of the odds of unfavourable outcomes among development group. Next the independent validation of the scale based on data from 96 emergency department patients after TBI was done.

Results: The scale consist of four independent predictive parameters such as age, Glasgow Coma Scale (GCS), systolic blood pressure (SBP) and Marshall computed tomography (CT) classification. The scale provides a score in the range from 0 to 6 points, where 0 is the best result. The scale score ≤ 2 predicted full recovery, which was confirmed by a ROC curve analysis with the area under the curve (AUC)=0.931 (excellent accuracy) and by Youden's index of 0.7222. The validation also confirmed that the discriminative ability of the model was adequate (AUC=0.936).

Conclusion: Our scale has good performance and could be a future clinical tool in predicting the recovery outcome of patients who suffered TBI without surgical treatment.

Keywords: Traumatic brain injury; Predictors head trauma; Outcome measures; Validation; Prognostic scale; Glasgow Outcome Scale (GOS)

Introduction

Traumatic brain injury (TBI) is called a "silent epidemic" [1] and still represents the leading cause of disability among people under the age of 45 in the world [2]. TBI is a public health problem affecting an estimated 200-300 cases per 100 000 people each year [3].

Based on literature published after the year 2001, traumatic brain injuries have been divided into four types: mild, moderate, severe and critical. The main criterion which determines the type of TBI is the patient's score on the Glasgow Coma Scale (GCS). Despite the fact that mild traumatic brain injury (mTBI) accounts for 80-90% of traumatic brain injury cases, patients with TBI are a very heterogeneous group. They are characterised by various disease processes which are connected with complex and unclear pathophysiology. Thus, a primary mechanical injury to the brain initiates metabolic and inflammatory processes which exacerbate the primary traumatic injury to neurons, leading to secondary brain damage [4]. Understanding the main components of the destructive cascade in secondary brain injury and finding prognostic factors may be a good foundation to develop novel approaches in managing patients with TBI.

Over the past 30 years, interest in the search for predictive models of brain injury has increased. The seminal paper which discussed a statistical model with which one could predict the outcomes following head injury was proposed by Teasdale and Jennett [5] allowing for the quantification of the impairment of consciousness. In subsequent years the key papers on the prediction model include those by Narayan, Signorini and Hukkelhoven [6-8]. Currently several large reliable prognostic models are available which were developed on large data sets in accordance with the latest methodological insights. The best-known models were developed by the International Mission on Prognosis and Analysis of Clinical trials in Traumatic brain injury database (IMPACT models) [9], the Corticosteroid Randomisation After Significant Head Injury trial data (CRASH models) [10]. The Trauma Audit and Research Network (TARN) database and the Transforming Research and Clinical Knowledge in TBI (TRACK-TBI) [11].

The models use various combinations of prognostic factors, but all of them emphasize the value of age, GCS and pupillary reactivity as

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the most important predictors concerning TBI patients. The available models included different subgroups of patients subjected to different treatment procedures including surgical treatment, which is known to improve the short- and long-term clinical outcome. However, a large number of patients with TBI from Glasgow Coma Score 14-15 do not ultimately require neurosurgical intervention [12]. The predictive models presented in the literature provide limited knowledge about prognosis in TBI patients conservatively treated.

Objective

In our study, we focused on a population of patients suffering from different degrees of brain injury without immediate neurosurgical intervention thus representing a special subgroup. Our goal was to create a simple prognostic scale for clinicians to predict the outcome of TBI patients conservatively treated.

Methods

This study was performed in the Department of Neurology with Neurology Intensive Care Unit and the Emergency Department (ED), a tertiary academic medical care centre in Lublin, Poland. The target group for this study were closed–head injury patients aged ≥ 18 years with different degrees of TBI without immediate neurosurgical intervention. Moreover, the inclusion criteria were as follow: time of head trauma no longer than 48 hours before examination, first brain injury in lifetime, computed tomography (CT) scan performed and basic clinical and laboratory assessment done on admission. The exclusion criteria were serious comorbidity (advanced cancer, severe hepatic and renal failure) and injury to other parts of a body rated with Abbreviated Injury Scale (AIS) score of equal or above than 4, with represents the threshold for a severe injury, visible in CT scan acute hematomas exhibit thickness beyond 15 mm for epidural and beyond 10 mm for subdural hematomas. The study was divided into two stages. The creation of the prognostic scale for TBI was the first stage of this study. It was done based on completed data taken from 184 patients admitted to the Department of Neurology in the years 2008-2013. During this period there were a total of 240 consecutive eligible closed-head patients. However, seventeen patients were excluded because data on functioning outcome at 6-month was unavailable, ten patients were excluded because they clinical data were incomplete, twelve patients because they went through a neurosurgery treatment, eleven patients had significant intracranial pathologic changes before their injury and six patients had serious comorbidity or serious injury of other parts of a body.

The second stage of this study was the validation of the scale using the same criteria. From 119 consecutive eligible patients in TBI admitted to the ED in the years 2014-2015, completed data from 96 of them were used for model validation. An outcome at 6-month post admission to ED was not obtained from fourteen patients. Five patient required sudden surgical evacuation of hematomas so they were also excluded. Three patients were excluded because of the serious comorbidity and one patient was excluded because of old posttraumatic changes in CT scan. Figure 1 presents a flow diagram of development and validation group.

In order to select the best parameters for creating the scale we recorded demographic and epidemiologic characteristics. We focused on age, gender, causes of injury, the presence of polytrauma and their severity (based on Injury Severity Score-ISS) and other medical conditions. The clinical characteristics considered on admission were blood pressure, state of consciousness assessed by the Glasgow Coma Scale.

CT scans of the study population were assessed in accordance with the Marshall computed tomography (CT) classification with supplement of category (VII) [13]. According to the Marshall CT classification, the discriminative features in categories are:

- Intracranial pathology seen on CT scan - Absence (class I)/ Presence (Class II-VII),
- High or mixed density mass lesions >25 cc - Absence (Class II-IV)/Presence (V-VI),
- Compression of basal cisterns - Absence (Class II)/presence (III-IV),
- Degree of midline shift with the cut-off point being 5 mm (Class II-III less than 5 mm and class IV >5 mm),
- Focal lesion - Surgical evacuated (Class V)/not surgical evacuated (Class VI).
- Brainstem contusion or unknown classification of lesion seen on CT scan (Class VII).

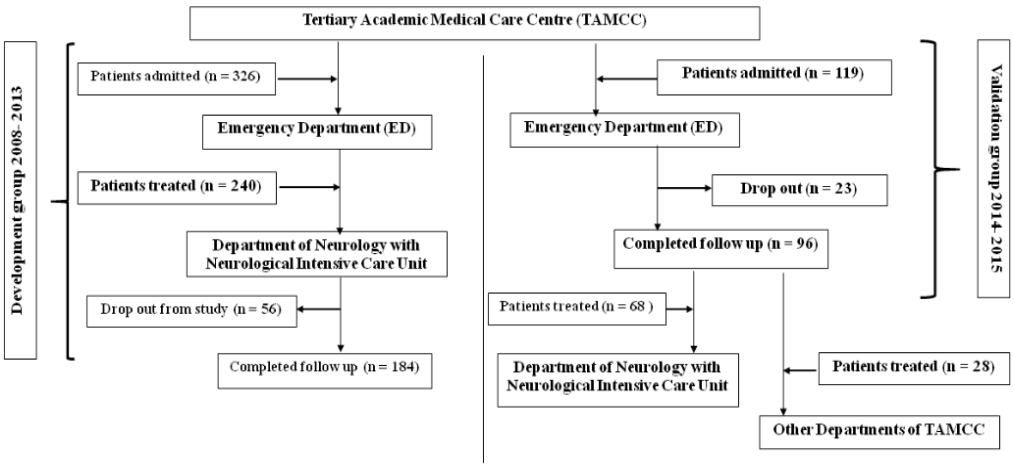

Figure 1: Flow diagram of development and validation group.

We also collected the values of such laboratory parameters as glucose, sodium, potassium, haemoglobin, platelet count, prothrombin time and leukocytes. The parameters listed above were collected within the first hour after hospital admission.

The validation group was assessed according to the proposed scale. Outcomes of both test groups were assessed using the dichotomized Glasgow Outcome Scale (GOS) at six months after injury:

- Full recovery outcome (GOS=5)
- Unfavourable outcome (GOS ≤ 4).

The information about patients' outcomes was obtained in two ways directly during a follow-up visit 6 months after suffering TBI and by a telephone interview of patients or their relatives. The study was approved by the hospital's institutional review board no KE 144/2010. Moreover, each participant of the focus groups signed written informed consent form in accordance with the Declaration of Helsinki.

Statistical Analysis

Expression of collected data was dependent on the type of variables. Continuous variables were presented as means, standard deviation, and range and categorical variables were reported as counts and percentages.

For a comparison of proportions, Fisher's exact test or the Chi-square test of 13 factors in relation to the six month dichotomized outcome (full recovery and unfavourable outcome) was applied where appropriate. Continuous variables were analysed with the use of the Student's t-test if they were normally distributed, or with the Mann-Whitney U test if they were non-normally distributed.

All potential predictors with the significance level of $p<0.05$, identified in a univariate analysis, were included in the multivariate models. A multivariate logistic regression analysis was carried out using backward elimination to identify independent predictors ($p<0.05$).

For the purpose of creating a model, all continuous variables were categorized into meaningful categories based on ROC curve analysis and literature review. The selection of categories accepted on the scale has been confirmed by the percentage distribution of the outcome depending on the scale criteria. The relative weighting of each individual component of the scale was determined from the relative change of the odds of unfavourable outcomes among development group. The performance of the model was assessed in terms of discrimination and calibration, the Hosmer-Lemeshow goodness-of-fit test and ROC curve with an area under the curve (AUC) with an optimal cut-off point were applied, respectively. At the end we performed a validation of the scale using the ROC curve analysis with a quantitative description of the proposed scale in order to predict a full recovery outcome. All the statistical analysis was done using software Medcalc 12.2 (Ostend, Belgium).

Results

Patients characteristics

Tables 1 and 2 present the demographics and clinical characteristics of two cohorts of TBI patients. Mild traumatic brain injury (mTBI) patients (GCS 13-15) represented the largest group (80.44% of the development group vs. 86,46% of the validation group). According to the inclusion and exclusion criteria the first examined group consisted of 184 patients. Amongst them 63.59% (117 patients) were men and 36.41% (67 patients) were women, with a calculated ratio of 1.8:1. In the second group of 96 patients the male/female ratio was 2.1:1 (65 men (67.71%)/31 women (32.29%)). The age distribution of patients with TBI (Figure 2) revealed that the highest occurrence was in the age group of 18–30 years (28.26% of vs. 32.29%), followed by 51-60 years (20.11% of the development group) and 61-70 (16.67% of the

Variables	Development group	Validation group
Age [(mean+-SD, (range)]	47.1 ± 20.3 (18-95)	48.7 ± 21.9 (18-90)
Female/Male [n (%)]	67 (36.41%/117 (63.59%)	31 (32.29%)/65 (67.71%)
Head AIS [(mean+-SD, (range)]	2.44 ± 1.27 (1-5)	2.59 ± 1.31 (1-5)
1-2	102 (55.43%)	54 (56.25%)
≥3	82 (44.57%)	42 (43.75%)
Presence of multi-trauma [n (%)]	51 (27.72%)	23 (23.96%)
Injured body region (%)		
Head/Neck	100%	100%
Face	23%	27%
Chest	17%	9%
Abdominal or Pelvic Contents	13%	15%
Extremities or Pelvic Girdle	41%	37%
External	52%	61%
Injury severity (poly-trauma patients)	8.84 ± 6.89 (2-33)	9.57 ± 6.51 (2-41)
ISS 1-8 [n (%)]	56.86%	51.14%
ISS 9-15 [n (%)]	23.53%	27.36%
ISS > 15 [n (%)]	19.61%	21.5%
Injury mechanism [n (%)]		
falls	66 (35.87%)	47 (48.96%)
Accidents	64 (34.78%)	20 (20.83%)
Violence	30 (16.30%)	8 (8.33%)
others (not classified)	24 (13.04%)	21 (21.88%)
Alcohol intoxication [n (%)]	32 (17.39%)	16 (16.67%)
Co-morbidity		
Diabetes	2 (1.09%)	1 (1.04%)
Hypertension	12 (6.52%)	9 (9.38%)
Hyperlipidemia	10 (5.43%)	6 (6.25%)
Coronary artery disease	3 (1.63%)	2 (2.10%)
Atrial fibrillation	4 (2.17%)	5 (5.21%)
Thyroid disease	2 (1.09%)	3 (3.13%)

Table 1: Demographical and clinical characteristics of the two cohorts of TBI patients.

Prognostic variables		Mean. range (development group n=184) excluding Marshall CT and GCS	Mean. range (validation group n=96) excluding Marshall CT and GCS
Glucose (mg/dl)		103 (57-310)	101 (66-184)
Sodium (mmol/l)		140 (103-152)	141 (122-154)
Potassium (mmol/l)		4.19 (2.1-5.4)	4.1 (3.1-5.5)
Haemoglobin (g/dl)		13.6 (8.50-17)	13.50 (6.5-17.7)
Platelet count (x10^3/microliter)		251 (39-871)	226 (83-685)
Prothrombin time (seconds)		11.96 (9.92–31)	11.25 (9.3-16.6)
Leukocytes (x10^{3}microliter)		8.53 (3.30-21.98)	8.72 (3.44-23.5)
Marshall CT	I-II	145 (78.81%)	67 (69.79%)
	III-VII	39 (21.19%)	29 (30.21%)
GCS	≤ 12	36 (19.57%)	13 (13.54%)
	13-14	37 (20.11%)	29 (30.21%)
	15	111 (60.33%)	54 (56.25%)
SBP (mmHg)		134 (90-200)	130 (110-167)
DBP (mmHg)		80 (40-120)	79 (53-112)
MABP (mmHg)		105 (65-160)	105 (86-138)

Table 2: Clinical characteristics of the two cohorts of TBI patients.

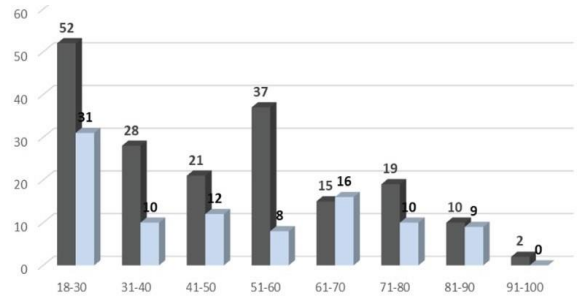

Figure 2: Age distribution with respect to time of brain injury.

validation group). In this study men (Age 44 years for the development group and 45 years for the validation group) had a lower mean age of morbidity compared to women (Age 52 and 56 years).

The most frequent causes of TBI in the tested groups were falls (35.87% in the first group vs. 48.96% in the second group), traffic accidents (34.78% vs. 20.83%) and violent attacks (16.30% vs. 8.33%). Presence of injuries to other areas of the body was found in 27.72% vs. 23.96%. The incidence of body parts injuries was presented in Tables 1 and 2. The most frequent diagnoses within face were nasal fracture and/or mandibular fractures without dislocations (almost 60% in each tested group). Approximately 80% of abdominal injuries have been categorized as a mild liver and/or spleen contusions. Regarding the types of chest injuries, patients had mostly mild trauma such as rib fractures (55% including multiple in 31% vs. 62% including multiple in 27%) and other fractures like collarbone, sternum or scapula (24% vs. 21%). Other diagnoses included pulmonary contusions (12% vs. 10%) and small pneumothorax (9% vs. 7%). Regarding the ISS score the majority of patients (above 50% in both groups) received score in the range 1-8. The most frequent comorbid illness in both groups was arterial hypertension 6.52% of the development group vs. 9.38% of the validation group and hyperlipidemia is 5.43% vs. 6.25%.

In the development group, we found more patients with GCS ≤ 12 compared to the validation group, in which we found more patients with categories III-VII Marshal CT. Despite the fact that the validation group was twice smaller, it was comparable to the development group.

Univariate and multivariable analysis

Table 3 shows the results of the univariate analysis of patient's characteristics on admission, which were previously reported as important predictors in literature. The study identified a considerable relationship between conventional covariates such as glucose, hemoglobin, prothrombin time, leukocytes, age, Marshall CT classification, GCS, blood pressure (systolic-SBP, diastolic-DBP, mean-MABP) and 6 month GOS.

The multivariable analysis confirms the strength of independent prognostic factors in TBI. Amongst them are: age, Marshall CT classification, GCS, SBP, DBP, MABP and several laboratory parameters such as glucose, hemoglobin, leukocytes and prothrombin time.

Subsequently, the scoring system compressed to four parameters with the strongest statistical significance in order to simplify the model (Table 4). The excluded laboratory parameters revealed worse statistical significance compared to the factors included in the model: glucose (p=0.0091), leukocytes (p<0.012), prothrombin time (p=0.023) and hemoglobin (p<0.048). Systolic and mean blood pressure have also shown a strong predictive value (p<0001). Considering the simplicity

Prognostic variables		p-value	Odds ratio	95% CI
Glucose (mg/dl)		p=0.038	0.99	0.98 to 0.99
Sodium (mmol/l)		p=0.295	1.04	0.97 to 1.11
Potassium (mmol/l)		p=0.554	1.21	0.67 to 2.31
Hemoglobin (g/dl)		p=0.012	1.26	1.05 to 1.51
Platelet count (×10³/microliter)		p=0.477	0.99	0.99 to 1.00
Prothrombin time (seconds)		p=0.048	0.86	0.73 to 1.01
Leukocytes (×10³/microliter)		p=0.025	0.90	0.81 to 0.99
Age (years)		p<0.0001	0.29	0.14 to 0.57
Marshall CT	I-II	p<0.0001	0.06	0.02 to 0.14
	III-VII			
GCS	≤ 12	p<0.0001	1.46	1.28 to 1.67
	13-14			
	15			
SBP (mmHg)		p=0.0001	0.97	0.95 to 0.98
DBP (mmHg)		p=0.0004	0.95	0.93 to 0.98
MABP (mmHg)		p<0.0001	0.96	0.94 to 0.98

Table 3: Univariate predictors influencing final outcome.

Variables included in model	Coefficient	SE	OR	p-value
Age	-1.47748	0.48393	0.2282	0.0005
Marshall CT	-2.22594	0.51914	0.108	<0.0001
Systolic blood pressure	-0.023157	0.011095	0.9771	<0.0001
Glasgow Coma Scale	0.31713	0.086754	1.3732	0.008

Table 4: Multivariable predictors of full recovery.

of the scale we decided to choose SBP. For diastolic blood pressure (DBP) p value was p=0.0004.

Prognostic scale for traumatic brain injury

Based on the results of the uni- and multivariable analysis, literature review and authors' experience as clinicians, a prognostic scale for TBI patients was created. As it was mentioned above four meaningful parameters such as age, GCS, SBP and Marshall CT classification create the scale. The statistical analysis allowed us to select such scale components so that their weights and effects on the scale were very similar. This is a necessary requirement to create a simple prognostic scale. Proper selection of factors with similar weight for the scale allowed to assign the same score 0 for each scale element with the strongest association with full recovery. Grades in the model increased successively when the probability of unfavourable outcome (odds) increased for the assigned categories in the model. The method of assigning score to the category on the scale is presented in Table 5.

Figure 3 shows a percentage distribution of the outcome depending on the changing scale criteria. The scale provides a theoretical score in the range of 0 - 6 points. In the scale we adopted that 0 points for each parameter was the most favourable. The least favourable parameters were rated as 1 point for age and SBP and for factors like GCS and Marshall CT classification the worst score was 2 points. 0 points was given to patients aged under or equal to 60 years, 15 points in GCS, systolic blood pressure in the range of 110-150 mmHg and I-II points in the Marshall CT classification. One point was given for age above 60 years, GCS between 13-14 points, systolic blood pressure below 110 mmHg and above 150 mmHg and a Marshall CT classification of III-VI points. Two points were given for GCS ≤ 12 points and Marshall CT classification VII. The scale is presented in Table 6.

Internal and external validation of the prognostic scale

The demonstration of the outcome distribution amongst the

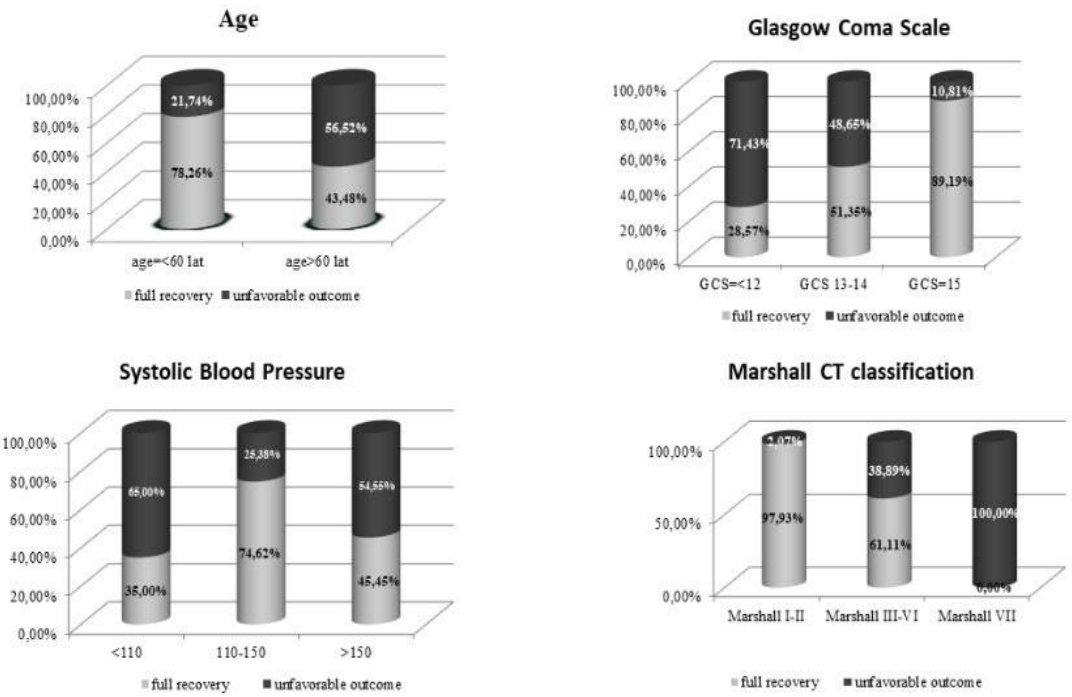

Figure 3: Distribution of the outcome depending on the scale criteria.

	Prognostic scale score	0	1	2
Odds	Age	≤ 60	>60	
		0.28	1.30	
	Marshall	I-II	III-VI	VII
		0.21	1.77	-
	SBP	110-150	<110 - >150	
		0.35	1.20	
	GCS	15	13-14	≤ 12
		0.14	1.06	2.60

Table 5: Odds for unfavorable outcome among the development group.

Traumatic Brain Injury Scale	
Age of patients	
≤ 60 years	0 point
>60 years	+1 point
GCS	
15 points	0 point
13-14 points	+1 point
≤ 12 points	+2 points
Systolic blood pressure	
110 – 150 mmHg	0 point
< 110 or > 150 mmHg	+1 point
Marshall CT classification	
I-II	0 point
III – VI	+1 point
VII	+2 points

Table 6: The simple prognostic scale in traumatic brain injury.

individual scores of the traumatic brain injury scale for 2 cohorts is presented in Table 7 and Figure 4 which shows that equal or less than to 2 points in the TBI scale would predict a full recovery outcome.

Number of points in the scale points	Full recovery [n (%)]	Unfavourable outcome [n (%)]	Death [n (%)]
0	63/64 (98.44%)	1/64 (1.56%)	--
	30/30 (100%)	--	--
1	49/51 (96.08%)	2/51 (3.92%)	--
	27/28 (96.43%)	1/28 (3.57%)	
2	28/35 (80%)	7/35 (20%)	--
	16/19 (84.21%)	3/19 (15.79%)	--
3	3/19 (15.79%)	15/19 (78.95%)	1/19 (5.26%)
	3/12 (25%)	7/12 (58.33%)	2/12 (16.67%)
4	1/11 (9.09%)	8/11 (72.73%)	2/11 (18.18%)
	1/5 (20%)	4/5 (80%)	--
5	--	2/3 (66.67%)	1/3 (33.33%)
	--	1/1 (100%)	--
6	--	--	1/1 (100%)
	--	--	1/1 (100%)

Table 7: Distribution among the individual scores of the traumatic brain injury scale for both test groups.

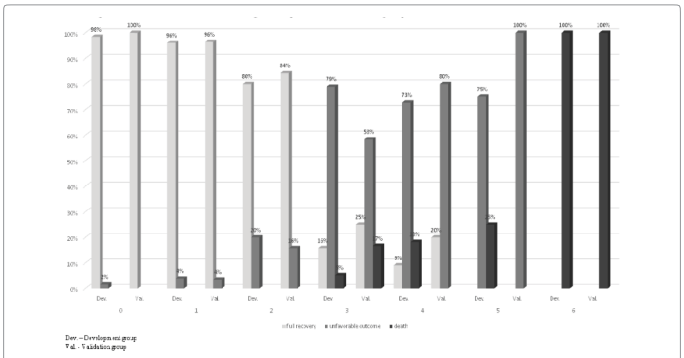

Figure 4: Distribution of outcome among development and validation group in accordance with scale score.

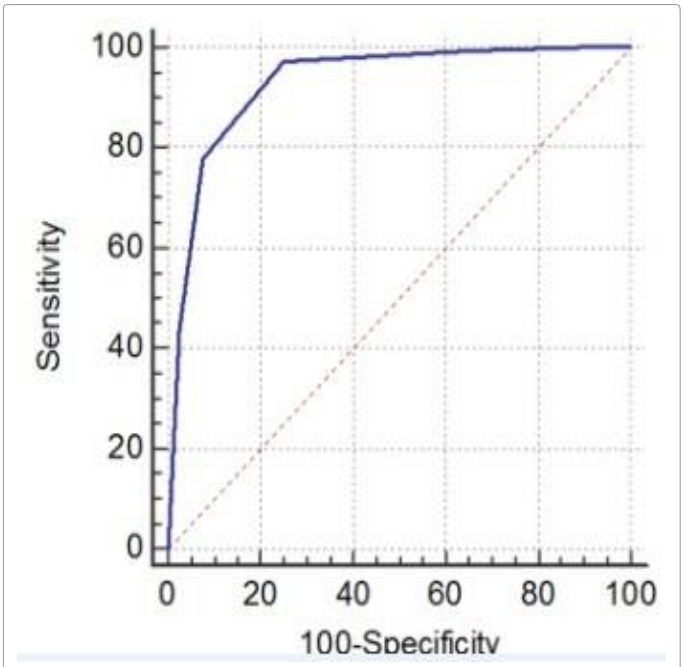

Figure 5: The ROC curve analysis of the development group for proposed scale.

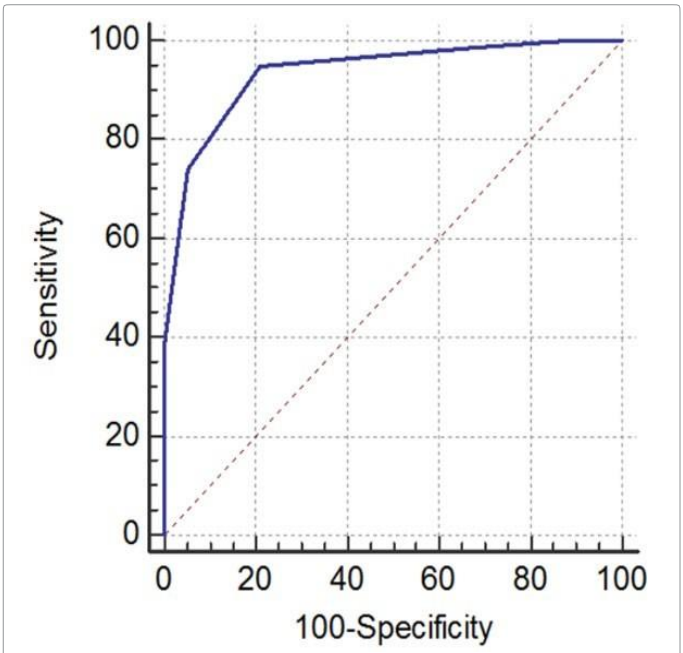

Figure 6: The ROC curve analysis of the validation group for proposed scale.

The receiver-operating characteristic curve analysis for the prediction of a full recovery outcome showed an optimal cut-off point less than or equal to 2. The scale score ≤ 2 predicted a full recovery outcome, which was confirmed by the ROC curve analysis with an area under the curve (AUC)=0.931 (excellent accuracy) and by Youden's index of 0.7222. The independent validation also confirmed that the discriminative ability of the model was adequate (AUC=0.936). The quantitative description of the ROC curve analysis for both test groups are shown in Table 8 and also in Figures 5 and 6.

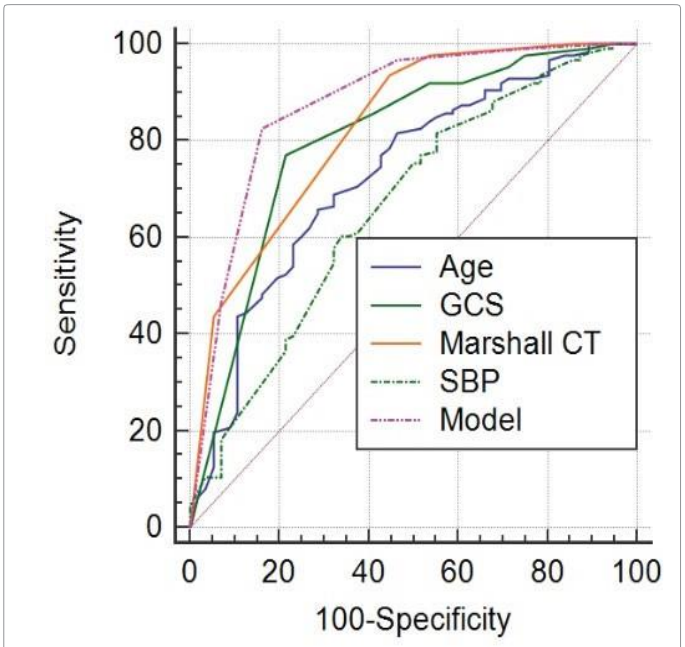

Figure 7: Comparison of the ROC curve analysis for the prognostic scale and individual parameters of the scale.

Results of the First Group Analysis	
Area under the ROC curve (AUC)	0.931
Standard Error	0.0247
95% Confidence interval	0.884 to 0.963
Significant level P	<0.0001
Youden Index	
Youden index J	0.7222
Associated criterion	≤ 2
Sensivity	97.22%
Specifity	75.00%
Positive predictive value	93.30%
Negative predictive value	88.20%
Results of the Second Group Analysis	
Area under the ROC curve (AUC)	0.936
Standard Error	0.0278
95% Confidence interval	0.867 to 0.976
Significant level P	< 0.0001
Youden Index	
Youden index J	0.7375
Associated criterion	≤ 2
Sensivity	94.81%
Specifity	78.95%
Positive predictive value	94.81%
Negative predictive value	78.95%

Table 8: Results of the ROC curve analysis for the prediction of a full recovery outcome regarding the proposed scale.

Figure 7 and Table 9 show values of the ROC curve analysis for the prognostic scale compared to the ROC curve analysis for the separate individual components of the scale like Marshall, GCS, SBP and age.

Discussion

In this study we established a new simple scale in order to predict the outcome for patients with different degrees of brain injury without

Prognostic Scale	
Area under the ROC curve (AUC)	0.931
Standard Error	0.0247
95% Confidence interval	0.884 to 0.963
Sensitivity	97.22%
Specificity	75.00%
NPV	88.20%
PPV	93.30%
LR+	13.93
LR-	0.76
Marshall	
Area under the ROC curve (AUC)	0.830
Standard Error[a]	0.0304
95% Confidence interval[b]	0.767 to 0.881
Sensitivity	93.75
Specificity	55.36
NPV	18.9
PPV	98.8
LR+	2.10
LR-	0.11
GCS	
Area under the ROC curve (AUC)	0.803
Standard Error[a]	0.0347
95% Confidence interval[b]	0.738 to 0.858
Sensitivity	77.34
Specificity	78.57
NPV	28.6
PPV	96.9
LR+	3.61
LR-	0.29
SBP	
Area under the ROC curve (AUC)	0.709
Standard Error[a]	0.0438
95% Confidence interval[b]	0.637 to 0.773
Sensitivity	92.80
Specificity	47.46
NPV	16.4
PPV	98.3
LR+	1.77
LR-	0.15
Age	
Area under the ROC curve (AUC)	0.819
Standard Error[a]	0.0381
95% Confidence interval[b]	0.755 to 0.872
Sensitivity	99.19
Specificity	62.30
NPV	22.6
PPV	99.9
LR+	2.63
LR-	0.13
[a]Development group; [b]Validation group	

Table 9: The ROC curve analysis for the prognostic scale and individual parameters of the scale.

immediate neurosurgical intervention. We have limited knowledge about the impact of conservative treatment to prognosis in this group of patients. Moreover, a different pathophysiology of brain injuries after neurosurgical treatment determines the need to create a prognostic model for patients treated conservatively. Points-based outcome-scoring systems are popular amongst physicians as they permit a rapid assessment of a patient's prognosis. Our 6-point scale suggests that patients with initial punctuations of 3 or more points in the score should be managed differently compared with the standard care of those with fewer points. More than 80% of patients with TBI conservatively treated, who received 2 or less points in our model fully recovered. The decision point and the predictive strength of the proposed model was uniquely confirmed in the validated group by a ROC curve analysis with the area under the curve AUC=0.936 (excellent accuracy). Predicting the occurrence of a full recovery over time is an important issue in clinical medicine.

In our center about 2% of advice given in Emergency Departments is associated with head injury. About 80% of them are mild traumatic brain injury (GCS 13-15) and 20% moderate and severe. The percentage of distribution, of head trauma severity was similar in the training sample from the Department of Neurology and validation cohort from ED. In the United States the same distribution was observed [14].

Four parameters like: age, SBP, GCS and Marshall classification, used to create the scale are reliable independent predictors with $p<0.05$ and what is more, they are easy to use. Comparing our model to two currently known prognostic models for TBI patients (IMPACT and CRASH models), it is important to point out that the characteristics of the study groups were quite different. As mentioned above our model was developed on a dataset, on the vast majority of patients with mild traumatic brain injury with a high proportion of patients with GCS 15 (about 75% of mTBI group). The IMPACT model was developed on a trial dataset with a patient who sustained moderate and severe TBI. The CRASH model includes all TBI severity groups (development population GCS 3-14 points), also different than our study group. Lingsma has done validation of CRASH models on patients with mild head injury and the result was unsatisfactory (AUC 0.49–0.50) but when patients with GCS 15 were excluded, discrimination of the CRASH models were better. Previously proposed models for patients with head trauma recognize GOS 4 (mild disability) as beneficial. Prediction of a full recovery outcome in mTBI imposes the need to recognize GOS 4 as an unfavourable result.

In summary our model is dedicated to patients after head injury who were disqualified from urgent surgical treatment. Our purpose is to help clinicians at the beginning to determine the probability of a full recovery in TBI patients qualified for conservative treatment. It is known that there is a risk of delayed neuro-surgical intervention in patients with acute traumatic brain injury. Fu-Yuan revealed that from a group of 340 patients with acute mTBI 3.8% of them required delayed neuro-surgical intervention [15]. However, this was associated with characteristic features in CT scans inter alia with larger volume of hematomas. We excluded patients with a high risk of having surgery within 48 hours with a visibility in the CT scan of acute hematomas exhibiting a thickness beyond 15 mm for epidural and beyond 10 mm for subdural hematomas. In the validation group none of them needed delayed neurosurgical treatment. The components included in this promising model with reference to the literature are discussed below.

Age at the time of injury is amongst the most important predictive factor for patients with TBI. The strong relationship between age and outcome in TBI has been demonstrated in many previous prognostic studies with the older patients demonstrating a worse outcome [10,16-18]. Most studies have documented threshold values varying from 30 to yearsofage [16]. In this study, age > 60 years correlated with an unfavourable outcome.

The next prognostic factor was blood pressure. Patients after TBI

have an impaired autoregulation mechanism of cerebral perfusion pressure. This probably explains why both high and low blood pressure is related to higher mortality [19]. Low values of blood pressure lead to diminished cerebral blood flow and then to brain ischemia. Likewise, high values of blood pressure seem to be as detrimental as ischemia because hyperemia may be followed by immediate post-traumatic ischemia, edema as well as secondary brain hemorrhage [19].

We observed the prognostic effects for blood pressure and a 6 month outcome. The patients with SBP between 110-150 mmHg on admission have a better outcome. Both lower and higher values were associated with a poorer outcome. These findings were used as one of the criteria of our scale. A similar result was obtained from the IMPACT study with SBP in the range of 120-150 mmHg indicating greater chances of a better outcome [20]. Zafar demonstrated that SBP in the range of 120-140 mmHg reduced mortality amongst patients with severe and moderate TBI [21]. In this study we also determined the favourable range of DBP and MABP. For DBP it ranges from 60 to 95 mmHg and for MABP the values are 85-115 mmHg. The Butcher study provides evidence that the mean arterial blood pressure between 85 to 110 mmHg correlated with a favourable outcome [20].

The neurological assessment on admission was performed using GCS, a quick and practical system for assessing the level of a patient's consciousness. For a long-time GCS was found to be one of the strongest predictors in TBI [10,17]. However, the use of GCS at admission is of limited prognostic value, particularly for patients with mild head injury [22]. In literature, the cases of patients rated GCS above 12 are defined as mild. Some authors suggest that a GCS score of 13 cannot be considered as mild traumatic brain injury [23,24]. The main point of reference during triage patients with TBI in ED is GCS scoring. Patients receiving 15 points according to a GCS score are assigned as low treatment priorities. Our study presents that 89,19% of patients with 15 points according to a GCS score fully recovered contrary to patients with 13-14 GCS points among whom only 51.35% fully recovered. In cases of patients with a GCS score ≤ 12 points only 28,57% of them fully recovered. In accordance with statistical analysis we used unconventional categorization of GCS score (15, 13-14, ≤ 12) in our model.

The last very strong predictor in the scale is Marshall CT classification. Most of the patients in the study group who were classified into I and II Marshall CT class had fully recovered. This is in agreement with previous studies done on a group of 5209 patients [25]. Derivation of new prognostic models for TBI patients including the Marshall Classification becomes more feasible by using assigned supplement to Marshall Classes. Therefore, in our model we applied VII classes of Marshall classification to aid in a clinical application. Class VII is as a separate category in our scale what was explicitly confirmed in statistical analysis.

In addition to the above-mentioned predictors of scale, our study confirmed the strong predictive value of laboratory parameters commonly known with wide documented predictive value such as: Value of glucose, level of leukocytes, level of hemoglobin value, prothrombin time. Despite the strong independent predictive value, they were not included in our model for two reasons. Firstly, our challenge was to create a simple model, which in our reasoning meant: optimal number of components, only widely known and available predictors, user-friendly scoring with clear categorization of dichotomized outcome forecasts (full recovery and unfavourable outcome). Secondly, the multivariate analysis showed a slightly lower predictive value of laboratory parameters compared to the factors included in the model.

Summing up, the prognostic model can predict outcomes much more accurately than prognosis based on the widely known separate predictive components or clinicians' experience [26]. Our comparative ROC curve analysis confirm differences in the prognostic accuracy of the prognostic scale and its separate components. Although the positive predictive value (PPV) is higher for the separate components, other indicators such as: negative predictive value (NPV), likelihood ratio of a positive and negative test result (LR^+ and LR^-) for the model are significantly better than for each of the component. The ROC curve analysis for the prognostic model demonstrates added value of score calculation instead of using individual components separately (AUC is the highest for the prognostic scale).

In medicine, prognosis is central, which means that one of the fundamental responsibilities of all clinicians is to provide information about prognosis of the outcome of a TBI [27].

Our model demonstrates a promising clinical outcome scoring system. Using a non-standard and easy-to-use categorization of parameters, has given hopeful results for predicting full recovery in the significant subgroup of patients after T BI. Moreover,our study can also serve as a background to a number of secondary analyses to find an optimal prognostic tool for TBI patients conservatively treated. The independent validation of the predictive accuracy of the TBI scale is warranted to further strengthen the validity of this promising scoring system. The scale would be a reliable diagnostic test with high predictive values for a full recovery outcome (AUC=0.936, Youden index=0.7375), and is characterised by high sensitivity as well as high specificity [28].

However, as each predictive model, our scale has some limitations. The data used for development and validation of the scale were analysed retrospectively and came from two departments, located in a single-centre. Among the validation group there were no patients requiring delayed neurosurgical treatment. The correlation between the proposed model and the risk of delayed neurosurgical intervention were not analyzed. It is a fundamental issue which we should bear in mind that a GOS score is a simplified approach to evaluate the outcome after TBI. Therefore, taking this into account we are planning to use Extended Glasgow Outcome Score (GOSE) as a more-sensitive outcome measure.

Conclusion

Despite the limitations listed above, our model demonstrates a promising clinical outcome scoring system for predicting a full recovery outcome of patients after TBI conservatively treated. This was confirmed by the independent validation of the scale. The strength of our prognostic scale is that it would enable clinicians to directly estimate the probability of a full recovery for patients who suffered TBI on admission in the emergency department. What is more, this scale might be helpful for clinicians to provide information to a patient and relatives on the expectation of outcome and to plan the level of monitoring, duration as well as the necessity for hospitalisation and the intensity of treatment.

Conflict of Interest

None of the authors have any financial or non-financial competing interests.

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