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EVALUATION OF CLINICAL VERSUS IMAGING PREDICTOR MODELS OF HEAD INJURY OUTCOME

Anaesthesiology

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ABSTRACT

Background: Traumatic brain injury (TBI) is a global health problem and a leading cause of mortality and morbidity. The therapeutic interventions are usually based on the assessment of prognosis of TBI patients. There are not many studies comparing the predictability of clinical and investigational parameters based models. We have contemplated a study to evaluate the clinical and imaging regression models and assessing and comparing the clinical versus imaging models.

Methods: 100 patients were enrolled. 10 clinical variables and 3 imaging variable were recorded. Initially all the variables were analyzed and ranking was done. The clinical variables selected were age, GCS, pupillary reaction to light, reparatory rate, anisocoria and SBP (systolic Blood Pressure) and imaging variables selected were the petechial hemorrhages, obliteration of third ventricle or basal cisterns and midline shift depending upon 'p' value of <0.05. Two models clinical and imaging were developed using binary logistic regression analysis. Both the models were assessed by sensitivity, specificity, accuracy, Hosmer - Lemeshow test and AUC (area under the curve) of ROC (receiver operating characteristic curve) curve. The internal validation of the two models was done by estimation of error rate, crossvalidation and bootstrapping. The models were compared by 'Z' test.

Results: The sensitivity, specificity, accuracy and AUC of ROC of the clinical model are 98%, 76%, 94% and 0.94 respectively. The sensitivity, specificity, accuracy and AUC of ROC of the imaging model are 85%, 100%, 99% and 0.91 respectively. The sensitivity, accuracy and AUC of ROC are higher in clinical model whereas the specificity is more with imaging model. The internal validation and 'Z' test revealed no significant difference between clinical and imaging models.

Conclusions: The clinical model gives an equally good estimation of prognosis and useful particularly at site of injury or any natural disaster for triage.

KEYWORDS

Head injury, Clinical model, Imaging model and Comparison of predictive models

Introduction

Traumatic brain injury (TBI) is a global health problem with an approximate incidence of 0.2– 0.5% each year. It is a leading cause of mortality, morbidity, and socioeconomic losses in India. Approximately 1.6 million individuals sustain TBI and seek hospital care annually in India. [1]

Clinicians decide therapeutic interventions based on their assessment of prognosis of TBI patients. Many doctors believe that an accurate assessment of prognosis is important when they made decisions about the use of specific methods of treatment which may be hyperventilation, barbiturates, or hyperosmolar therapy. At the same time the assessment help in deciding whether or not to withdraw treatment. It plays as important role in counselling the patients and relatives.[2]

Commonly used clinical predictors of outcome of TBI both individually or in combination are age, Glasgow coma scale score, pupillary reactivity, extra cranial injury, hypoxia and hypotension, brain stem reflexes .The investigational predictors are based on CT findings, like midline shift, petechial haemorrhages and obliteration of third ventricle or basal cisterns.[3]

There are many studies predicting the outcome in severe head injuries taking into consideration both the clinical and investigational parameters. However, there are not many studies comparing the predictability of clinical and investigational parameters based models.

Clinical parameters are equally important, particularly at the site of an accident or at the place of disaster, where investigation facilities are not available. We have contemplated a study to evaluate the clinical and imaging parameters by developing logistic regression models. Then assessing and comparing the clinical and imaging models.

Material and Methods

After Institutional ethical and research committee clearance 100 patient who had head injury at our emergency were enrolled into our study and followed up to 14 days.

Sample size was estimated as suggested by Miller and Kunce [4], the subject to predictor ratio of 10 to 1. Therefore 100 patients were selected taking into consideration the initial clinical variables.

The clinical variables and CT scan findings were recorded and transformed in to binary data a following manner : age <40 as '1' ≥ 40 as '0' , female as '0' and male as '1', systolic blood pressure (SBP) <100 mmHg as '1' ≥ 100 as '0' and diastolic blood pressure (DBP) < 60'1' ≥ 60 as '0' in mm Hg ,pulse rate (beats/minute) <100 as '1'and ≥ 100 as'0' ,respiratory rate/minute(RR) <20 as '1' and ≥ 20 as '0',GCS < 8 as'0' ≥ 8 as '1',pupillary reaction to light present as '1' absent as'0', anisocoria yes as '1' no as '0', extra cranial injury yes as '1' no as'0' and CT findings , midline shift <5mm as '1' ≥ 5mm as '0' petechial haemorrhages yes as '1' no as '0' , obliteration of third ventricle or basal cisterns yes as '1' no as'0', The outcome of head injury was measured by Glasgow outcome scale on 14th day as follows 1) Discharges home without neurological sequelae 2) Discharged home with neurological sequelae favorable as '1' and 3) Severe disability 4) Vegetative state 5) Death as unfavorable as '0'.

Initially all the variables were analyzed and ranking was done by using the Tanagra datamining software [5] using Fisher filtering with a p value of < 0.05 (Table 1). The clinical variables selected were age, GCS, pupillary reaction to light, reparatory rate, anisocoria and SBP. The imaging variables selected were the petechial hemorrhages, obliteration of third ventricle or basal cisterns and midline shift depending upon 'p'value of <0.05. The clinical six variables namely age, GCS, pupillary reaction to light, respiratory rate, anisocoria , SBP and the Imaging variables midline shift , petechial haemorrhages , obliteration of third ventricle or basal cisterns were taken and two models clinical and imaging were developed using binary logistic regression analysis.

The two models were assessed by sensitivity, specificity and accuracy. Hosmer -Lemeshow test is used for calibration of models. (Figs.1 - 2) and discrimination is by AUC (area under the curve) of ROC (receiver operating characteristic curve) curve. (Fig. 3) (Table 2)

The ability to predict correctly is one of the most important criteria to evaluate classifiers in supervised learning. The preferred indicator is the error rate (1 - accuracy rate).

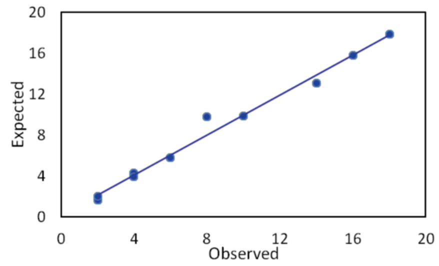

Figure 1: The calibration by H-L test for Clinical Model

Table 1: Showing the p-value of different variables

S.No	Variable	p-value
1	GCS	0.000
2	Pupil reaction to light	0.000
3	Respiratory rate	0.000
4	Age	0.026
5	Anisocoria	0.027
6	SBP	0.027
7	DSP	0.570
8	Puse rate	0.823
9	Extra cranial injury	0.944
10	Sex	0.947
11	Petechial haemorrhages	0.000
12	Obliteration of 3rd ventricles or Basal cisterns	0.000
13	CT midline shift	0.006

It states the probability of misclassification of a classifier. The first estimator, the simplest, is the resubstituting error rate.

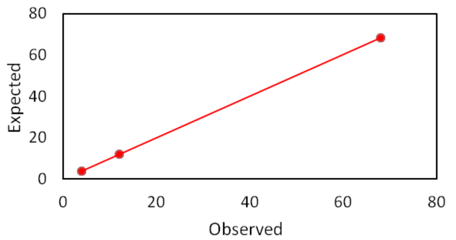

Figure 2: The calibration by H-L test for Imaging Model

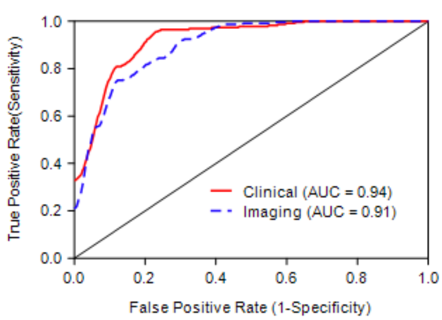

Fig 3: ROC graphs for clinical and imaging model.

Table 2: Comparison of Clinical and Imaging models

Model	Sensitivity	Specificity	Accuracy	Area of ROC	Hosmer-Lemeshow –p-value
Clinical	98 %	76%	94%	0.94	0.5611
Imaging	85 %	100 %	90 %	0.91	0.8863

It calculates the percentage of misclassified sets on the training .The resubstitution error rate is highly optimistic. It underestimates the true error rate because the same datasets were used for training and testing the classifier. This drawback can be alleviated by splitting the data into two parts: the first called training (or learning) set (e.g. 2 / 3) is used to create the classifier; the second, called the test set (e.g. 1 / 3), is used to estimate the error rate. It is unbiased. We have divided the datasets, into 60 % to train and 40% to test to find out the true error rate. (Table 3) When we deal with a small sample size, dedicating a part of the dataset to the test phase penalizes the learning phase, and moreover the error estimation is unreliable because the test sample size is also small.

Thus, in the small sample context, it is preferable to implement the resampling approaches for error rate estimation, like the crossvalidation (CV), bootstrap. All of them are based on the repeated train test process, but in different configurations. The aim is to evaluate the error rate of the classifier created on the whole sample. Along with the resubstitution error rate, the data was divided into train and test and the error rate calculated on the test datasets in our study.

Table 3: Prediction error rate estimation

Prediction error estimation method	Clinical Model	Imaging Model	Difference between the models
Resubstitution	0.0500	0.0833	0.0333
Test (TRUE)	0.0588	0.0588	---
Crossvalidation	0.1100	0.1100	0
.632+ Bootstrap	0.1345	0.1405	0.0066
.632 Bootstrap	0.1224	0.1328	0.0104

The crossvalidation (CV) and bootstrap methods were also used in the two models. (Table 3). Finally the AUCs of the two model were compared by using Z test. (Table 4). [1,6]

Table 4: Z test to compare AUC of two models

Model	Standard error	Difference in AUC	Z Value	p-two tailed
Clinical	0.0236	0.034	0.7174	0.473128
Imaging	0.0411			

Results

Mean age the patients was 32.2 with standard deviation of 12.62 and ranging from 12 to 61 years. Male (88%) population had head injury more than female patients (12%) (Table 5). The CT findings and the diagnosis is shown in the (table 6).

Estimated logistic regression clinical model for neuro outcome 1 = -2.73 + (0.028 x Age) – (0.99 x Anisocoria) + (4.47 x GCS) + (0.50 x Pupil reaction) + (0.31 x RR) + (0.94 x SBP).

Table 5: Descriptive Statistics of Clinical Variables

Variable Name	Mean ± SD	Minimum Value	Maximum Value
Age in years	32.22 ± 12.62	12	61
SBP mm Hg	120 ± 20	90	180
DSP mm Hg	76.6 ± 12.16	60	110
Puse rate beats /minute	87 ±62	58	110
Respiratory rate beats /minute	18.± 4.6	14	32
GCS (Median)	13	3	15

Estimated logistic regression imaging model for neuro outcome 1= 3.21 + (0.63 x CT. Medline shift) – (3.30 x CT Petechial haemorrhage) – (2.61x Obliteration of 3rd ventricles or Basal cisterns).

Table 6: Diagnosis of 100 cases and the frequency

Diagnosis	Frequency
Mild head injury	18
Moderate head injury	36
Severe head injury	18
EDH	12
SAH	4
Cerebral oedema	4
Depressed fracture	4
Lacerations	2
Contusions	2
Total cases	100

The sensitivity, specificity, accuracy and AUC of ROC of the clinical model are 98%, 76%, 94% and 0.94 respectively. The sensitivity, specificity, accuracy and AUC of ROC of the imaging model are 85%, 100%, 99% and 0.91 respectively. The sensitivity, accuracy and AUC of ROC are higher in clinical model whereas the specificity is more with imaging model.(Table 2)(Fig.1) The Hosmer –Lemeshow test was not significant in both the models, confirming good calibration in both the models (Figs 2-3). Therefore both models have good calibration and discrimination

The supervised learning of the both models were measured by error rate otherwise called internal validation. The resubstitution error rate, and the test sample error are (TRUE) were similar in both the models. The error rates with resampling methods like crossvalidation and bootstrapping in both the model found have minimal difference. (Table3) When compared the AUCs of both the models by Z test, there is no statistical difference found. (p>0.05) (Table 4).

Discussion

Traumatic brain injuries (TBI) are a real social problem because of industrialization and motorization [1]. Two million individuals each year sustain traumatic brain injury in the United States, resulting in 56,000 deaths. [2]

It is becoming a major cause of death and disability. Establishing a reliable prognosis after injury is difficult. On the other hand, clinicians treating patients often make therapeutic decisions based on their assessment of prognosis. Many prognostic models have been reported but none are widely used. [7]

We have developed two prognostic models one is dependent on only clinical variable and other investigational variables of CT imaging for predicting clinically relevant outcomes in patients with traumatic brain injury. The models have excellent discrimination and good fit with internal validation methods.

The clinical model variables were similar to crash study, however in our study the respiratory rate, anisocoria are found to have significant effect on TBI outcome, which were not there in many of the outcome studies of TBI.

The major extra-cranial injury which is one of the clinical variable in crash study, but in our study, it was not significantly effecting the outcome (p value =0.944). TBI causes dysautonomia manifested by episodes of fluctuations in blood pressure (BP), pulse rate (PR), respiratory rate (RR), were associated with poorer outcomes (8). In our study we have found that systolic blood pressure and respiratory rate were significantly effecting the outcome. Age was associated with unfavorable outcome particularly after 40 years, lower GCS also found to be in linear relationship with mortality. [2,9] Similarly in our study we found age above 40 and low GCS have significant effect on outcome. Pupillary reactions like absence of or abnormal pupillary reactions were found to be associated with worse outcomes in TBI [9,10] and it is same in our study.

In our imaging model, CT. midline shift, CT petechial hemorrhages and obliteration of 3rd ventricles or basal cisterns are found to have significant prognostic value as with previous studies. [8,9,11]

The clinical model sensitivity, accuracy and AUC of ROC curve in fact are better comparted to imaging model. The error rates by resubstitution, test set, cross validation and bootstrap methods are almost similar in both the models. However the specificity is better with imaging model. When compared with Z test there is no significant difference between the two models. The clinical model gives an equally good estimation of prognosis and is useful particularly at site of injury or any natural disaster for triage.

Limitations: Our study is not a multicentre study. The external validation was not performed in a different locations or centres.

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