Outcome Predictors of Severe Head Injury at Zagazig University Hospital

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ABSTRACT

BACKGROUND: Outcome prediction after severe traumatic brain injury has major clinical importance especially in countries like Egypt with increased trauma indices.

OBJECTIVES: This work aims to evaluate simple admission variables, transcranial doppler pulsitality index and s100 b protein and their ability to predict the outcome of traumatic brain injury.

PATIENTS AND METHODS: A prospective study that took place at the neurotrauma unit at Zagazig University hospital (from august 2013 to march 2016) and included 240 patients with severe traumatic brain injury with (GCS ≤ 8) ; transcranial doppler pulsitality index has been measured in 85 Patients of them in the first ,second and third day. Serial S100 b protein samples have been collected from 33 patients. The collected data included age, sex, type of trauma , GCS , best motor response , blood pressure , pupil reactivity , CT Marshall score and associated injuries . Patients with severe extra cranial injuries, extremes of age and who died within 24 hours have been excluded. Outcome was evaluated using Glasgow outcome score (G.O.C) at the time of discharge and after 6 months. Madras head injury prognostic scale (MHIPS) was calculated for each patient and correlated with the G.O.C.

RESULTS: Significant association between the G.C.S , best motor response , pupil response , hypotension , CT Marshall score , third day PI , MHIPS and G.O.C . Significant weak indirect correlation between Glasgow coma scale, Best Motor Response, Madras Head Injury Prognostic scale and Glasgow Outcome Scale (r=-0.346, -0.402 & -0.489 respectively) while a significant weak direct correlation between CT score, first day PI, second day PI, third day PI and Glasgow Outcome Scale (r=+0.229, +0.224, +0.235 & +0.366 respectively).

CONCLUSION: Most of study parameters proved their effectiveness in prediction of the outcome. MHIPS proved to be simple , rapid and effective in outcome prediction of severe TBI. Transcranial Doppler PI proved its significance for mortality prediction.

KEY WORDS: severe traumatic brain injury , pulsitality index , S100 b protein , Madras head injury prognostic scale , outcome.

Introduction

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Traumatic brain injury (TBI) is considered a worldwide leading cause of mortality and disability is predicted to surpass many diseases as a major cause of disability and death by the year 2020.[1] Outcome prediction after severe head injury is an area of intense interest for neurosurgeons. Traumatic brain injury outcome is usually assessed at one , three , six or twelve months after incident. Most of patients (about 85%) recover within the six months period, however, further recovery can occur after this period. The most commonly used globally as TBI outcome measure is the Glasgow outcome scale (GOS).[2] The pattern of outcome distribution mostly has a U-shaped curve, with the majority of patients either died or fully recovered. Some clinicians further classify outcomes into favorable (moderate disability or good recovery) versus unfavorable (death, vegetative state, or severe disability).[3] In the past decades many TBI prognostic models have been created, with various methodological methods The importance of these models is its ability to can provide a scientific basis for informing relatives about the life expectancy , facilitate prognostic classification and validate the comparative studies ,evaluating the clinical management and statistical analysis of the randomized controlled trials.[4] Madras Head Injury Prognostic Scale (MHIPS) with six major prognostic factors. Each prognostic factor was divided into 3 subgroups, according to prognosis. The subgroup factor with the best prognosis has been assigned a score of (3) , the subgroup with the worst prognosis (1) and the middle subgroup (2). The maximum total score is 18 and the minimum total score is 6.[5]

Commonly used predictors of outcome both individually or incombination include age, Glasgow coma scale score, pupillary reactivity, hypotension, CT Marshall core. [6] Transcranial Doppler (TCD) is a non-invasive method, which provides assessment of cerebral blood flow through a cerebral artery and an increased pulsatility index (PI) would be associated with a poor outcome.[7]

S100 b protein released by astrocytes has been shown their direct correlation with the traumatic brain injury situations as these could be released in response to oxidative stress, inflammation, cerebral blood flow irregularities, apoptosis and cell death.[8]

Patients and Methods

A prospective study that took place at the neurotrauma unit at Zagazig University hospital (from august 2013 to march 2016) and included 240 patients with severe traumatic brain injury with (GCS $\leq$ 8) ; transcranial doppler pulsitality index has been measured in 85 Patients of them in the first ,second and third day. Serial S100 b protein samples have been collected from 33 patients. The collected data included age, sex, type of trauma , GCS , best motor response (BMR) , blood pressure , pupil reactivity , CT Marshall score and associated injuries . Patients with severe extra cranial injuries, extremes of age and who died within 24 hours have been excluded. Outcome was evaluated using Glasgow outcome score (G.O.C) at the time of discharge and after 6 months. Madras head injury prognostic scale (MHIPS) was calculated for each patient and correlated with the G.O.C.

Statistical analysis:

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All data were collected, tabulated and statistically analyzed using SPSS 20.0 for windows Quantitative data were expressed as the mean ± SD & median (range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Continuous data were checked for normality by using Shapiro Walk test. Kraskall Wallis H test was used to compare more than two groups of non-normally distributed data. Post hoc test was done by Mann Whitney U test to compare between two groups of non-normally distributed data. Percent of categorical variables were compared using Pearson's Chi-square test or Fisher's exact test when was appropriate. Trend of change in distribution of relative frequencies between ordinal data were compared using Chi-square test for trend. Spearman's rank correleation coefficient was calculated to assess relationship between various study variables, (+) sign indicate direct correleation & (-) sign indicate inverse correleation, also values near to 1 indicate strong correleation & values near 0 indicate weak correleation. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values of PI and S100 with maximum sensitivity and specificity for prediction of GOS score 1 (good recovery). Area Under Curve (AUROC) was also calculated, criteria to qualify for AUC were as follows: 0.90 – 1 = excellent, 0.80-0.90 = good, 0.70-0.80 = fair; 0.60-0.70 = poor; and 0.50-0.6 = fail. The optimal cutoff point was established at point of maximum accuracy. Univariate logistic regression analysis was done to detect predictors for GOS score 1 (good recovery) and 5 (death). All tests were two sided. p-value < 0.05 was considered statistically significant (S), p-value < 0.001 was considered highly statistically significant (HS), and $p \geq 0.05$ was considered statistically insignificant (NS).

Results:

Demographic data: male was the predominant (76.7%), 64.6% of the patients were between 15-45 years old. Mean age was 28 years; range 3-68 years, the major type of trauma was road traffic accidents RTA (70.4%).

Clinical predictors: For G.C.S ,The most frequent score was score 8 (34.2%) while the least frequent score was score 5 (5.4%). For best motor response, The most frequent score was score 5 (40%) while the least frequent score was score 1 which was found in 14 patients (5.8%). For pupil reactivity, 67% of patients had both pupils equal and react to light while 16.7% had one reactive pupil and 16.3% had neither reactive pupils. About 25% of the studied patients had hypotension at initial presentation. About 75 patients (31.2%) had associated injuries as fasciomaxillary trauma, skin wound, superficial skin contusions etc... Long bone fracture was the most frequent associated injuries (19.2%). The least frequent associated injuries were vertebral fracture (0.8%). Lung contusion had occurred in 7.5% of the studied patients.

Radiological predictors: for Marshall CT score , The most frequent score was score 3 which was found in 110 patients (45.8%) while the least frequent score was score 1 which was found in 2 patients (0.8%). The Transcranial Doppler Pulsitality index (PI) *had been measured in 85 patients with 242 readings* ; using Siemens ACUSON X300 ultrasound system equipped with P 4-2 phased array 2-4 MHZ probe applied

to transtemporal window The mean at first day was 1.57 and median was 1.58, range 0.68 – 2.7. At 2nd day the mean was 1.3±0.37 and the median was 1.26; range 0.72 – 2.74. At 3rd day the mean was 1.1±0.25 and the median was 1.04; range 0.72 – 1.89.

Laboratory predictor: There were 96 Samples of S100 b protein collected from 34 patients. Assay range was 50-1500 ng/l At the 1st day the mean 459.6±389.55 ng/l and the median was 390; range 25– 1200 ng/l. At 3rd day the mean was 404.54 ± 369.53 ng/l while the median was 390; range 0 – 1200. At 5th day the mean was 416.8±378.74 ng/l while the median was 207; range 23 – 1100 ng/l.

Prognostic scales: The Mean score was 12.80±2.65 while the Median score was 13; range 7 – 18 . The most frequent (MHIPS) was score 6-12 (44.2%) while the least frequent score was score 15-18 (31.7%). The most frequent G.O.C was 5 (death) (49.2%) while the least frequent outcome was 3 (severe disability) (7.9%). Good recovery had occurred in only 22 patients (9.2%).

Correlation between study predictors and G.O.C: There was Insignificant association between sex and Glasgow Outcome Scale which was 9.2% of male versus 8.9% of female had good recovery while 50.5% of male versus 44.6% of female were died (P=0.7), According to the age, there was 10% of patients had good recovery versus 50% died at group (<15 years old), 9% of patients had good recovery versus 48.4% died of age group (15-45 years old) while there was 8.6% of patients had good recovery versus51.4% died in age group >45 years. (P =0.8). Mean age in good recovery group was 26.31years while in died group was 28.53 years and difference between them was insignificant (p=0.4). there was an insignificant association with Glasgow Outcome Scale (p=0.4) where 15.4% of direct trauma had good recovery versus 13.3% of fall from height and 7.1% of RTA while 38.5% of direct trauma was died versus 46.7% of fall from height and 51.5% RTA. A significant association between GCS and Glasgow Outcome Scale(P<0.001) where 15.9% of patients with GCS of 8 had good recovery versus 7.1% of patients with GCS of 3 while 34.1% of patients with GCS of 8 was died versus 85.7% of patients with GCS of 3 (P=0.003), also these significant differences were present between other pairs. A significant association between best motor response and G.O.S. (P < 0.001) where 13.5% of patients with score 5 had good recovery versus 7.1% of patients with score 1 while 32.3% of patients with score 5 died versus 85.7% of patients with score 1 (P=0.005), also these significant differences were present between other pairs. A significant association between pupil reaction and G.O.C (P=0.004). A significant association between hypotension and G.O.C (P <0.001) as 8.9% hypotensive group patients had had good recovery versus 41.3% died. An insignificant association between associated injuries and G.O.C (P =0.6) but there is a significant association between lung contusion and G.O.C (p=0.04) as 83.3.% of patients of patients with lung contusion died versus 46.4% of patients of patients without lung contusion (P=0.02). As for initial CT score , in good recovery patients there were 11.1% of patients with CT score 6 versus no patients with CT score 1 while in death group, 83.3% of patients

with CT score 6 versus no patients with CT score 1 (P=0.001). These significant differences were also present between other pairs. As for TCD PI, At the 1st day, the mean PI reading was 1.21±0.34 versus 1.64±0.47 in died patients and 1.60±0.35 in vegetative group (P=0.09). at the 2nd day the mean PI was 1.08±0.19 in good recovery group while it was 1.36±0.40 in died patients (P=0.099) an insignificant difference between different Glasgow Outcome Scale groups as regard second day PI (P=0.09). A significant difference between different Glasgow Outcome Scale groups as regard 3rd day PI (P=0.02) where PI was significantly higher in died group than good recovery group (Mean: 1.16 vs 0.94, P=0.009).For S100 b protein; At the 1st day, an insignificant difference between different Glasgow Outcome Scale groups (P=0.230) where mean S100 in good recovery group was 337.66 ng/l and in died group was 665.92 ng/l. At the 3rd the 5th day, there also was an insignificant difference between different GOS groups and mean S100 (P=0.4) and(P=0.9) respectively. Significant association between (MHIPS) and G.O.C (P<0.001). At score group 6-12, there 84% died versus 3.8% had good recovery while at Score 15-18, 25% died versus 21.1% had good recovery.

Using Spearman's correlation coefficient: A significant weak indirect correlation between G.C.S, Best Motor Response, MHIPS and G.O.C (r =-0.346, -0.402 & -0.489 respectively) while a significant weak direct correlation between CT score, 1st PI, 2nd PI, 3rd PI and G.O.C (r=+0.229, +0.224, +0.235 & +0.366 respectively).Also there was A significant direct correlation between CT score, GOS and 1st day PI (r=+0.629 & +0.224 respectively) while a significant indirect correlation between MHIPS and 1st day PI (r=-0.352).

Univariate logistic regression analysis potential predictors for G.O.C score 1 (good recovery): 1st day PI was a significant independent predictor for good recovery where probability of good recovery increase with decrease in 1st day PI (β=-0.258) as for 1 unit decrease in 1st day PI, about 13 times increase in the probability of good recovery (OR=0.076, p=0.024). MHIPS was a significant independent predictor for good recovery where probability of good recovery increase with increase in MHIPS (β=+0.323) as for 1 score increase in MHIPS, about 1.3 times increase in the probability of good recovery (OR=1.381, p=0.003).

PI as a predictor for GOS score 1 (good recovery); ROC curve Analysis:

Optimum cutoff of 1st day PI as a predictor for good recovery was ≤1.27 so 75% of patients with 1st day PI ≤1.27can be expected that they had good recovery, while 72.7% of patients with 1st day PI >1.27can be expected that they had outcome rather good recovery. Optimum cutoff of 2nd day PI as a predictor for good recovery was ≤1.30 so 100% of patients with 2nd day PI ≤1.27can be expected that they had good recovery while 49.4% of patients with 2nd day PI >1.27can be expected that they had outcome rather than good recovery. Optimum cutoff of 3rd day PI as a predictor for good recovery was ≤1.03 so 87.5% of patients with 3rd day PI ≤1.03can be expected that they had good recovery while 56.3% of patients with 3rd day PI >1.03can be expected that they had outcome rather good recovery, so we conclude that this cutoff is optimum to conclude good recovery

(patients with 3r day PI ≤1.03) than exclude outcome rather than good recovery (patients with 3r day PI >1.03). Among these different measurement 1st day PI is the best predictor for good recovery as its accuracy was 72.9% & AUROC was 0.760. While all measures of S100 b protein Couldn't predict good recovery.

Univariate logistic regression analysis potential predictors for GOS score 5 (death): GCS was a significant independent predictor for death where probability of death increase with decrease in GCS (β=-0.569) as for 1 score decrease in GOS, about 2.1 times increase in the probability of death (OR=0.468, P<0.001). Best Motor Response was a significant independent predictor for death where probability of death increase with decrease in Best Motor response (β=-0.760) as for 1 score decrease in BMR, about 1.7 times increase in the probability of death (OR=0.566, P<0.001). Pupil was a significant independent predictor for death where probability of death increase in neither reactive pupils patients (β=+1.517) as neither reactive pupils patients had probability of death about 4.5 times probability of death in both reactive pupils patients (OR=4.559, P<0.001).

Hypotension was a significant independent predictor for death where probability of death increase in hypotensive patients (β=+1.301) as hypotensive patients had probability of death about 3.6 times probability of death in non-hypotensive patients (OR=3.672, P<0.001). Lung contusion was a significant independent predictor for death where probability of death increase patients with lung contusion (β=+1.754) as patients with lung contusion had probability of death about 5.7 times probability of death in patients without lung contusion (OR=5.776, P=0.007)

CT score was a significant independent predictor for death where probability increase with increase in CT score (β=+0.360) as for score 1 decrease in CT score, about 1.4 times increase in the probability of death (OR=1.434, P=0.001). 3rd PI was a significant independent predictor for death where probability ncrease with increase in 3rd day PI (β=+2.192) as for 1 unit increase in 3rd day PI, about 8.9 times increase in the probability (OR=8.925, P=0.040).

First day S100 was a significant independent predictor for death where probability of death increase with increase in first day S100 (β=+0.002) as for 1 unit increase in first day S100, about 1 times increase in the probability of death (OR=1.002, P=0.019)

MHIPS was a significant independent predictor for death where probability increase with decrease in MHIPS (β=-0.434) as for 1 score decrease in MHIPS, about 1.5 times increase in the probability of death (OR=0.648, P<0.001).

ROC curve Analysis of PI as a predictor for GOS score 5 (death):

the optimum cutoff of 3rd day PI as a predictor for death was <0.97 so 86.5% of patients with 3rd day PI>0.97can be expected that they died in other hand 51.4% of patients with 3rd day PI≤0.97can be expected that they had outcome rather death, so we conclude that this cutoff is optimum to predict death PI>0.97 .

ROC curve Analysis of S 100 b protein as a predictor for GOS score 5 (death):

Optimum cutoff of 1st day S100 b as a predictor for death was >264 ng/l so 76.9% of patients with 1st day > 264 ng/l can be expected that they died while 65% of patients with 1st day ≤ 264 ng/l can be expected that they had outcome rather death.

Discussion

Demographic data;

As regard age:
The current study included 240 patients; mean age was 28 with range (3 – 68) years .
That was in agreement with:
Roozenbeek et al. (2013)[9] The demographic characteristics the International Mission on Prognosis and Analysis of Clinical Trials (IMPACT) Database. (n = 8509) the mean age was 30 with range (21-45) years .
in another major data set Corticosteroid Randomization After significant head injury (CRASH) trial (6681 patients) which recruited data from low and middle income countries the mean age was 32 with range (23 – 47).
Correlation between age and Glasgow Outcome Scale:
In our study we found that there was an insignificant association between age and G.O.C with mean age in the died group was 28.53 years.
These results were in agreement with:
Husson et al. (2010)[10] who systematically reviewed the prospective cohort studies stated that the evidence for the prognostic value of age was inconclusive and a larger proportion of studies found no association between age and outcome.
Sobuwa et al. (2014) [11]reported that increasing age was not associated with poor outcome in their analysis.
Imen et al. (2015) [12]reported that mean age didn't vary significantly between survivors and non survivors groups (p = 0.18).
CRASH Trial (2008)[13] reported that increasing age was associated with worse outcomes but this association was apparent only after age 40. However they found that increasing age had a worse prognosis in high income countries compared with low-middle income countries. This is because of even lower risks at younger ages in high income countries, while both have similar risks at older ages.
These results were in disagreement with:
Mosenthal et al. (2002)[14] reported that age itself is an independent predictor for mortality in TBI with increased mortality from TBI in the geriatric population.
Hukkelhoven et al. (2003)[15] compared various age groups and found continous associations between age and mortality and unfavorable outcome in patients with severe TBI. however these authors reported that arbitrary categorization of age and relatively small numbers of patients in specific age categories means that few patients can change proportion of poor outcome considerably.
Demetriades et al. (2004)[16] reported that there was a stepwise categorical relationship.
Maas et al. (2007)[17] reported in their external validation of the IMPACT study that age comes out as a powerful prognostic factor and older age was related to a worse outcome.
We could explain this disagreement
By the regional socioeconomic differences between countries and the

differences in mean age between different communities with the middle age population are the most prevalent.

As regard gender:

In the current study male percentage was 76.7 % .

Correlation between gender and Glasgow Outcome Scale:

In our study we found Insignificant association between sex and G.O.C

These results were in agreement with

Murray et al. (2007)[18] reported that their studies definitively show that no gender-related differences in outcome as assessed by the G.O.C exist in traumatic brain injury.

These results were in disagreement with:

Groswasser et al. (1998)[19] reported that females had better outcome .

Farace and Alves. (2000)[20] reported in their meta-analysis that females had poorer outcome. However they stated that there were small number in published reports about sex related differences as regard the outcome of TBI and careful, prospective study of sex differences in TBI outcome is clearly needed.

Farin et al.(2003) [21]stated that Female patients younger than 50 years tended to have worse outcomes, their explanation was that higher levels of estrogen relative to progesterone were considered as a possible explanation for the poorer outcome observed however , the difference was not statistically significant.

However, this theory was tested in further clinical trials ;

Skolnick et al ., 2014 [22] reported that their clinical trial results do not support the hypothesized superiority of progesterone treatment over placebo in patients with severe TBI.

Goldstein F et al ., 2017[23] reported that study of Protective Effects of Progesterone (ProTECT III) and Study of Progesterone in Severe Traumatic Brain Injury (SyNAPSE) have failed to prove the effectiveness of the progesterone as a neuroprotective drug for traumatic head injured patients.

As regard type of trauma:

In the current study the major type of trauma was RTA with 70.4%.

This was in agreement with

CRASH TRIAL (2008)[13] reported that upon comparing with patients from high income countries, those from low-middle income countries as regard the major type of injury in low-middle income countries was road traffic accident with 69.9 % while was 50.2 % in high income countries .

Clinical predictors

As regard the relation between G.C.S and GOC

Saadat et al. (2012) [24] reported that the GCS was a powerful predictor for TBI outcome with the (OR = .595 and p value < 0.001)

CRASH trial (2008)[13] reported that there was a clear linear relationship between GCS and mortality

Husson et al. (2010)[10] Systimatically reviewed the prospective cohort studies conducted from 1995 to 2008 and reported that low GCS on admission were strong predictors of poor outcome 6 months post-TBI

Udekwu et al. (2004)[25] reported that The GCS score is significantly related to both mortality and functional outcome in patients with head injury.

These results were in disagreement with:

Balestreri et al. (2004) [26]collected data between 1992 and 2001 and reported a

reduction in power of the GCS score as predictor of outcome after brain trauma and their study showed a loss in correlation between admission GCS and GOS. a significant correlation between the GCS and GOS for the first five years (overall 1992–1996: r = 0.41; p <0.00001; n = 183) and consistent lack of correlations from 1997 onwards (overall 1997–2001: r = 0.091; p = 0.226; n = 175).

We could explain this disagreement by the fact of the different pre-hospital patient care management between countries that more aggressive pre-hospital treatment, involving early sedation and intubation, can obscure the real GCS assessment. This problem in obtaining a valid neurological examination in the first 24 hours after trauma, as well as progress in clinical management, may have influenced the relevance of the GCS on outcome.

As regard the relation between Glasgow Coma Scale , best motor responce and Glasgow Outcome Scale

Our results showed a significant association between both GCS and best motor response with all groups of G.O.C (P < 0.001)

comparing predictive strength of G.C.S, best motor response

Their significant correlation was close to (r=-0.346, -0.402 respectively) and both had indirect significant correlation with G.O.C

These results were in agreement with

Healey et al. (2003)[27] reported that the motor component of GCS preserved almost all the predictive power of the GCS with the ROC (GCS) = 0.89, ROC (motor) = 0.87; (GCS) r = 0.42, motor response r = 0.40)

Beskind et al (2004)[28] compared the pre-hospital motor component of the Glasgow coma scale (GCS-m) to the pre-hospital total GCS (GCS-t) as a pre-hospital risk adjustment measure for trauma patients and they concluded that the pre-hospital m GCS appears have good discriminatory power and is equivalent to the pre-hospital t GCS for predicting outcome.

Lesko et al. (2013)[29] reported that both motor component and total GCS have the same predictive strength in their study.

Barker et al. (2014)[30] stated that estimation of a full GCS score based on eye opening and motor response for those who were intubated proved to be effective, as indicated by the fact that adding these estimated scores slightly improved and did not undermine the predictive utility of GCS and there is no change in the capacity of the GCS score to predict outcome over time.

Kupas et al. (2016)[31] reported that for all outcomes, the relative differences in specificity, sensitivity, and area under the receiver operation characteristic curve between motor score and total GCS score were clinically unimportant; therefore, they recommended the use of motor response assessment as a replacement for the total GCS score for field trauma triage.

As regard pupils:

In our study there was a significant association between pupil and outcome (P=0.004). Pupil reactivity was a significant independent predictor for death where probability of death increase in neither reactive pupils patients (β=+1.517) as neither reactive pupils patients had probability of death about 4.5 times probability of death in both reactive pupils patients (OR=4.559, p <0.001).

These results were in agreement with:

Lieberman et al. (2003) [43] concluded that Patients presenting with a GCS of 3

and Fixed Dilated pupils have no reasonable chance for survival.

Murray et al. (2007)[18] overviewed the IMPACT study database and reported that the pupil response to light is one of the most powerful predictors for the outcome.

Marmarou et al. (2007)[32] stated that the pupil reactivity is a powerful indicator for severe traumatic brain injury outcome.

Martins et al. (2009)[33] claimed that pupil examination at admission was independently associated with mortality in patients with severe TBI.

Majdan M et al. (2015) [34] compared pre-hospital and admission pupillary response and reported that their was no significant change in 84 % of cases and stated that the pupillary assessment at admission (AUC = 0.662; r = 0.214) performed best as predictors of 6 months mortality in their univariate analysis.

As regard the relation between hypotension and Glasgow Outcome Scale, our study showed a significant association between hypotension and G.O.C (P<0.001) with 72.1% hypotensive patients was died. Hypotension was a significant independent predictor for death where probability of death increase in hypotensive patients (β=+1.301) as hypotensive patients had probability of death about 3.6 times probability of death in non-hypotensive patients (OR=3.672, p<0.001).

These results were in agreement with **Andrew et al . (2002)[35]** reported that hypotension and low cerebral perfusion pressure (CPP) are the best predictors of death, with a 9.2% improvement in predictive accuracy (PA) than other variables in their study.

Jeremitsky et al. (2003)[36] studied the impact of hypotension in patients with severe TBI were compared to patients without severe TBI. mortality rate increased from 20 to 53% in severe TBI patients.

Murray et al. (2007)[18] reported that the presence of hypotension correlated significantly with a worse outcome

Imen et al . (2015)[12] reported that univarite analysis showed strong correlation between hypotension and mortality.

Spaite et al. (2016)[37] reported in their study on 13151 patients that the result of mortality with hypotesion was OR 2.5 [95% CI interval 1.9 to 3.3]

AS regard the relation between associated injuries and Glasgow Outcome Scale our study showed an insignificant association between associated injuries and outcome (P=0.571) where 6.7% of patients with associated injury had good recovery versus 10.3% of patients without associated injury while 56% of patients with associated injury was died versus 46.1% of patients without associated injury however, among the extracranial injuries studied

These results were in agreement with **Van Leeuwen et al. (2012)[38]** reported in their meta-analysis of the IMPACT, CRASH, and TARN databases that the extra-cranial injuries had less impact on outcomes of patients with severe TBI.

Leitgeb et al . (2013) [39]reported similar mortality rates between isolated TBI and TBI plus concomitant extra-cranial injury

These results were in disagreement with **Lefering et al. (2008)** [40] reported increased mortality rates in severe head injured patients concomitant with extra-cranial injuries

As regard lung contusion

Our study showed a significant association between lung contusion and Glasgow Outcome Scale (p=0.035).and lung contusion was a significant independent predictor for death where probability of death increase patients with lung contusion (β=+1.754) as patients with lung contusion had probability of death about 5.7 times probability of death in patients without lung contusion (OR=5.776, p=0.007).

These results were in agreement with **Baum et al. (2016)** [41] reported in their retrospective study of evaluation for the effect lung injuries sustained at the time of initial injury on the outcome. They claimed that traumatic lung injury a patient correlate significantly with poor outcome in severe TBI.

These results were in disagreement with **Leone et al. (2003)** [42] evaluated the impact on morbidity and mortality of pulmonary contusion in multiple-trauma patients with severe head trauma. In their study they concluded that the pulmonary contusion alters gas exchange but does not appear to increase the morbidity and mortality of multiple-trauma patients with head trauma.

However, ***this could be explained by*** the authors themselves who stated that a sample-size effect limited the interpretation in their study.

Radiological predictors

As regard the relation between CT score and Glasgow Outcome Scale our study showed a significant association between CT score and Glasgow Outcome Scale (p=0.001). CT score was a significant independent predictor for death where probability of death increase with increase in CT score (β=+0.360) as for 1 score decrease in CT score, about 1.4 times increase in the probability of death (OR=1.434, p=0.001).

These results were in agreement with **Munakomi et al. (2016)** [44]reported in their cohort study that Marshall can be used to reliably predict mortality in patients with acute TBI with high prognostic accuracy.

Deepika et al. (2015) [45]reported that the Marshall system has been shown to be a powerful predictor of outcome of TBI

Mata-Mbemba et al. (2014)[46] compared the performance of Marshall and Rotterdam CT scoring systems and individual CT findings included in these systems in predicting early death in patients with TBI. Both scores were significantly and positively associated with early death. Authors stated that the results led them to speculate that, although older than Rotterdam score, the performance of Marshall score, could be slightly stronger in predicting early death.

Maas et al. (2005)[47] reported that the Marshall CT classification had strong predictive power in their study, the presence of EDH was associated with a better outcome after trauma, which may be explained by the possibility of emergent surgical evacuation of such hematomas, however they concluded that further validation of this score is necessary, but the required data were not sufficiently available in most studies from IMPACT.

As regard the relation between Pulsatility Index (PI) and Glasgow Outcome Scale : 1st day PI was significantly higher in died group than good recovery group (Mean: 1.64 vs 1.21, p=0.013). Also in the 2nd day PI was significantly higher in died group than good recovery group (Mean: 1.36 vs 1.08, p=0.033). 3rd day PI was significantly higher in died group than good recovery group (Mean: 1.16 vs 0.94, p=0.009).

These results were in agreement with **Moreno et al. (2000)[48]** reported that the PI was statistically significant in both uni- and multivariate analyses. The mean PI predicting good outcome was 1, with 71% of their patients with a PI of less than or equal to 1 making good outcome. The mean PI predicting poor outcome was 1.56, with 83% of those with a PI of greater than or equal to 1.56 suffering poor outcome. In cases in which the PI was equal to or greater than 2.3 the mortality rate was 100%.

Tan et al. (2001)[49] reported that in a prospective study was conducted to evaluate the contribution of TCD ultrasonography to neurological outcome in a series of 96 severe traumatic brain injury patients and resulted in the mean PI in cases of good outcome (34 patients, 57%) was lower than 1.5 whereas in poor outcome (30 patients, 83%) was higher than 1.5 (P <0.001). And the authors concluded that TCD ultrasonography is valid in predicting the patient's outcome .

While **Trabold et al. (2004)[50]** performed TCD on arrival in the emergency room and stated that it may predict neurological outcome.the authors stated that The main result of their study was that a PI more than 1.31 was associated with a poor neurological outcome.

Calderon et al. (2006) [51] found a positive correlation between a PI value ≥ 1.0 measured by TCD and bad neurological outcomes in severe traumatic brain injury patients after statistical analysis they found that peak PI values ≥ 1.0 correlated positively to bad neurological outcomes as measured by GOS**.**

Gura et al. (2010)[52] found a strong significant positive correlation between increased PI and ICP in 1st , 3rd and 5th days and unfavorable outcome.

As regard correlation between PI and other study parameters

Our results showed a significant direct correlation between CT score, GOS and first day PI (r=+0.629 & +0.224 respectively)). this means that increased measurements of PI in first day were correlated with the CT score and worsening in the Glasgow Outcome Scale.

These results were in agreement with **Glaser et al. (2016)** [53]studied the correlation between PI and CT pathologies and in their study PI was higher in the CT-positive group. The number of patients with a PI value of >1.3 was also significantly higher in the CT-positive group.

Bouzat et al. (2016) [54]reported the significant correlation between admission CT and PI.

Ziegler et al. (2017)[55] studied TCD parameters including PI in severe TBI patients and reported that Patients with normal measurements can be expected to survive. Patients with hypoperfusion had a poor prognosis. Patients with vasospasm have a high incidence of mortality and severe disability. Therefore,TCD is useful in determining early prognosis.

Laboratory predictors

As regard Correlation between S100 b and Glasgow Outcome Scale: 1st day S100 b was a significant independent predictor for death where probability of death increase with increase in 1st day S100 (β=+0.002) as for 100ng/l increase in 1st day S100, about 1 times increase in

the probability of death (OR=1.002, p=0.019)**.**In our study Optimum cutoff of 1st day S100 b as a predictor for death was >264 ng/l so 76.9% of patients with 1st day S100 b >264 ng/l can be expected that they died in other hand 65% of patients with 1st day S100≤ 264 ng/l can be expected that they had outcome rather death

These results were in agreement with

Vos et al. (2004)[56] reported that S100 b protein were significantly higher in patients who died or had a poor outcome 6 months post injury than in those who were alive or had good outcome.

Da Rocha et al. (2006) [57] reported that patients with fatal outcome had higher mean S100 b concentrations when compared with survivors

Chabok et al. (2012)[58] reported that patients with unfavorable 3 months outcome had higher S100 b concentration on 3rd day (72 hours) than the ones with favorable outcome although levels decreased significantly 3rd day.

These results were in disagreement with

Olivecrona et al. (2009) [59] reported that their study clearly shows that the prognostic value of the S-100B for the prediction of mortality is low.

Nylen et al. (2008) [60] reported that in their analysis , the correlation is not strong enough to be used for prediction of outcome.

Unden et al . (2007)[61] reported that their study showed no association between the S-100B levels and prediction of outcome.

We could explain this conflict in our study; as the sample size of patients tested for S 100 b protein is relatively small (34 patients only) to the whole 240 patients included in our study which could create statistical difference.

As regard MHIPS validation

our study showed a significant association between MHIPS and Glasgow Outcome Scale (P<0.001) where 21.1% of patients with score 15-18 had good recovery versus 3.8% of patients with score 6-12 while 25% of patients with score 15-18 was died versus 87% of patients with score 6-12 (P<0.001), also these significant differences were present between other pairs e.g. good recovery group/vegetative group (P=0.048), moderate disability group/died group (P<0.001), severe disability group/died group (p<0.001) and vegetative group/died group (P<0.001) .

Also there was a significant difference between different Glasgow Outcome Scale groups as regard MHIPS (P<0.001) where mean MHIPS in good recovery group was 14.50 while in died group was 11.54 (P<0.001) ,where MHIPS was a significant independent predictor for good recovery where probability of good recovery increase with increase in MHIPS (β=+0.323) as for 1 score increase in MHIPS, about 1.3 times increase in the probability of good recovery (OR=1.381, P=0.003) MHIPS was a significant independent predictor for death where probability of death increase with decrease in MHIPS (β=-0.434) as for 1 score decrease in MHIPS, about 1.5 times increase in the probability of death (OR=0.648, P<0.001).Also , there was a significant indirect correlation between MHIPS and first day Pulsitality index (r= - 0.352).

These results were in agreement with

Yazdani et al. (2016) [62] reported that MHIPS has the ability to determine patient's prognosis in head trauma with high sensitivity and specificity.

Ebrahimi et al. (2016)[63] reported that there was a direct significant correlation

between the madras head injury prognostic scale scores in the early admission and final head trauma outcome based on GOS (P<0.001, r= 0.668).

Conclusion

G.C.S , pupil reactivity , hypotension and Marshall ct score are the strongest predictors for outcome of severe TBI. Both total GCS and its motor component had close predictive power so we recommend the use of the motor component of GCS as it avoids the misinterpretation in evaluating the eye and verbal responses of the G.C.S and its accurate prediction of mortality. In addition, we evaluated the utility of TCD in the context of severe traumatic brain injured patients Transcranial Doppler PI showed significant ability as a predictor for mortality especially on elevated PI in the continuous daily follow up. we have been able to externally validate a simple, easy to apply, and accurate bedside prognostication scale for head injury MHIPS, which can be used in any trauma center. we found highly significant correlation between most of study parameters and Glasgow outcome score.

summary

In our study we have been able to study the relationship between severe TBI outcome and simple admission characteristics and their ability to predict outcome in 240 patients with severe TBI. Also we studied the prognostic ability of TCD PI and S100 b protein and their correlation between the different study parameters.

Recommendations clinical judgment in deciding the management of an individual patient should not be swayed by the calculated prognostic score. The numbers involved in validation of S100β protein are still small. larger studies are required in our facility.

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