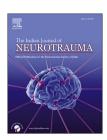


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Original Article

Early mortality predictor of severe traumatic brain injury: A single center study of prognostic variables based on admission characteristics

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ABSTRACT

Objective: Traumatic brain injury (TBI) is one of the leading cause of death in many developing countries. The intention of this study was to develop a predictor model - to identify high death risk of severely head-injured patients in an early period in order to plan an effective and efficient treatment strategy.

Method: We conducted a retrospective cross-sectional study with subjects of severe TBI patients (n=61) from 1st of January to 31st December 2010. Variables included age, gender, blood pressure, mean arterial pressure, pulse rate, respiration rate, temperature, Glasgow Coma Scale (GCS) score, motor response, choice of treatment and head computed tomography (CT) profiles. These models — then analyzed using multiple logistic regression. Results: The outcome of this study produced five factors that correlated significantly with the survival of these patients: compression in basal cistern, low motor response (<4), presence of intradural lesion, mean arterial pressure, and midline shift. We divided these factors into major and minor factor according to their contribution to survival. Compression of basal cistern compression and low motor response (<4) are the most significant factors in predicting mortality (sensitivity greater than 90%).

Conclusion: Basal cistern compression and motor response were the most valuable factors in determining the risk of death in severe TBI patients.

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1. Introduction

Traumatic brain injury (TBI) constitutes a critical public health and socioeconomic problem throughout the world. It is the leading cause of mortality and disability among young individuals in many countries. Worldwide, the incidence of TBI is rising sharply, mainly because of increasing motor vehicle use in low income and moderate income countries. TBI will

surpass many diseases as the major cause of death and disability by the year 2020. The incidence varies from 67 to 317 per 100,000 individuals and mortality rate range from around 4% to 7% for moderate injury to approximately 50% with severe traumatic brain injury. $^{1-3}$

In Indonesia, incidence of severe TBI is between 6 and 12% of all traumatic brain injuries with mortality rate ranging between 25 and 37%. Trauma data from our emergency

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department revealed 5.274 cases of trauma admission in which 2342 (44.4%) had a reported head injury. Mild head injury represented 68.9% of head injury, whereas moderate head injury with 20.96% and severe head injury was 10.1% of all head-injured patients.^{4,5}

Post TBI prognosis still remains a challenge to this day. Study of putative predictors are an active area of TBI research at present, and these studies are long-held concepts in the field that still remains really challenging. From socioeconomic standpoint, prognostic models with admission data are essential to support a cost-effective clinical decision making and facilitating reliable comparison for outcomes between different patient series and variation in results over time. Many studies have already described outcome following TBI and also - relate single variable to both global and detailed outcomes.^{6–9}

Our aim is simple, to develop a simple prognostic tool based on clinical and radiological characteristics to determine early mortality in severe TBI patients. This simple model can be used as an aid for prompt clinical decision making, and also provide better informed consent regarding patients prognosis for the family of these patients.

2. Clinical materials and method

2.1. Patient population and method

This cross-sectional retrospective study consists of 61 patients diagnosed with severe TBI (GCS < 9) treated in neurointensive care unit between 1st January and 31st December 2010. Patients below 14 years of age, multiple trauma patient with AIS \geq 3, GCS 3 and dilated pupils after resuscitation, admission > 8 h after injury, signs of aspiration pneumonia and without head CT Scan were excluded from this study. The reason for these exclusion criteria are to keep the data homogen, especially regarding the delayed response time in patient transportation which is an unfortunate common condition in third world and developing countries.

Information about injury severity was obtained from medical records and from data specifically collected for the purpose of the study. This data included the cause and nature of injury, age of patient, gender, GCS score after resuscitation, best motor response, physical findings (blood pressure, heart rate, rectal temperature), results of computerized tomography scans and also management of these patients. Based on their clinical data, patients were grouped into two groups; survived and unsurvived within 1 week period after admission. We intended to study the early mortality predictors of TBI solely from its demographic, clinical, and radiological data, without any bias from common intensive care unit (ICU) complications, such as pneumonia, urinary tract infection (UTI), and sepsis, etc, which commonly develops after 1 week of intensive care stay. 10,11

2.2. Statistical analysis

Data were processed on a personal computer by using commercially available statistic software. These variables were compared using chi square test with p value \leq 0.05. Only

significant prognostic factors were then summarized into a scoring system using multiple logistic regression test based on the odds ratio of each variable. This scoring system was tested for its specificity and sensitivity.

3. Results

From our study, we found a 65.5% mortality rate in 61 patients with severe traumatic brain injury after one week in hospital. Almost 80% of the patient were male (n=50) and only 20% were female (n=11). After analyzing various prognostic factors, as shown on Table 1, we — found a handful — variables that — significant statistically and related to mortality outcome ($p \le 0.05$). We found mean arterial pressure (MAP > 97.17 mmHg), motor response (\ge 4) and abnormalities on CT findings (compressed basal cistern, presence of intradural lesion, midline shift) to be statistically significant.

Table 2 shows a summary of these significant factors associated with mortality. In the early model, we took in all the statistically significant variables, such as; absent basal cistern, motor score, presence of intradural lesion, MAP, and midline shift > 5 mm. We evaluated these variables using the multiple logistic regression test and found that basal cistern to be the most dominant predictor with value of 2.860 followed by motoric response with value of 2.448. We simplified our scoring system and attributed basal cistern and motor response as major risk factors in predicting mortality, whereas presence of intradural lesion, MAP and midline shift as minor risk factors.

We further performed chi square test and logistic regression test with CI 95% and found significant correlation between major risk factors and mortality in these patients, as shown on Table 3. Presence of major factors (compressed basal cistern and low motoric score) had a sensitivity of 92,50% to predict mortality in the first week after severe TBI. In the unsurvived group, 37 (92%) of the total of 40 patients presented with either 1 major factor (73%) or two major factors (27%).

4. Discussion

TBI affects every communities, — age groups, and - societies across the world. Globally, the burden caused by TBI to patients, relatives, caretakers, and society is increasing. TBI is by definition, a heterogenous disease, and there are also important regional variations in epidemiology and outcome. Neurotrauma is a particular burden in developing countries, with the smallest capacity to manage it.^{2,3,8}

Prognosis is an essential element of medicine, and estimation of prognosis is a frequent component of clinical decision making. Therapeutic and diagnostic actions were aimed to improve prognosis. The science of clinical decision making and advances in statistical modeling have made it possible to be more confident about what is likely to happen and to consider prognosis in terms of probabilities rather than prophecies. The availability of large databases has opened new opportunities for an evidence-based approach to prognostic analysis. 8,11–13

Table 1 - Correlation between patient characteristics, physical findings, operative management and CT findings with mortality outcome. p Value Variables Survived (n = 21) Unsurvived (n = 40) OR (95%CI) Patient characteristics 0.091 2.75 (0.53-14.14) Male 19 (38.0%) 31 (62.0%) Female 2 (18.2%) 9 (81.8%) Age 2.55 (0.72-9.02) 0.139 36.30 (15.97) Average 27.48 (10.56) <40 17 (40.5%) 25 (59.5%) ≥40 4 (21.1%) 15 (78.9%) 0.75 (0.24-2.26) Management 0.61 Conservative 7 (30.4%) 16 (69.6%) Operation 14 (36.8%) 24 (63.2%) Time to operation 0.142 0.45 (0.15-1.32) 9 (47.1%) 25 (73.5%) <8 h ≥8 h 12 (44.4%) 15 (55.60%) Physical findings MAP 0.027 1.54 (1.01-2.36) 100.19 (18.64) Average 91.42 (17.48) <97.17 13 (50%) 13 (50%) >97.17 8 (22.9%) 27 (77.1%) Heart rate 0.596 1.33 (0.46-3.86) 88.85 (20.99) Average 83.86 (20.44) ≤87.13 20 (62.5%) 12 (37.5%) >87.13 9 (31.0%) 20 (69.0%) Respiration rate 0.377 1.67 (0.53-5.20) 24.35 (6.05) Average 23.86 (5.14) <24.18 15 (38.5%) 24 (61.5%) >24.18 9 (31.0%) 20 (69.0%) Temperature 0.194 2.28 (0.64-8.13) Average 36.85 (0.66) 37.20 (0.80) <37.08 17 (39.5%) 26 (60.5%) >37.08 4 (22.2%) 14 (77.8%) Motor response 0.000 2.29 (1.49-3.52) Average 4.48 (0.81) 3.93 (0.88) 19 (59.4%) 13 (40.6%) ≥ 4 < 3 2 (6.9%) 27 (93.1%) CT scan findings Hemorrhage Extradural 0.361 0.58 (0.18-1.87) Negative 14 (31.1%) 31 (66.9%) Positive 7 (43.7%) 9 (56.3%) Intradural 0.016 4.25 (1.25-14.46) Negative 9 (60%) 6 (40%) Positive 12 (26.1%) 34 (73.9%) SAH 0.703 1.67 (0.30-9.14) Negative 34 (64.2%) 19 (35.8%) Positive 6 (75%) 2 (25%) Basal cistern 0.000 9.33 (2.61-33.39) 9 (20.5%) Compressed 35 (79.5%) Uncompressed 12 (70.6%) 5 (29.4%) Midline shift > 5 mm 0.000 1.96 (1.32-2.92) Negative 18 (54.5%) 15 (45.5%) Positive 3 (10.7%) 25 (89.3%)

Information about prognosis and predictive statements can be useful in a number of ways. Concern about the probable outcome is the most important in the mind of relatives, and realistic counsel is therefore very important. — However, the greatest application of prognostic analysis is not at the level of the individual patient but rather at the "group"; even for quantifying and classifying the severity of

brain injury, as a reference for evaluating quality of care. 6,12,13

Mortality within one week was used in our study because death in - first - week is commonly because of the severity of TBI, whereas 30-day mortality or more could be related to complications of ICU stay, associated injuries (e.g. pneumonia, pulmonary embolism, sepsis, multiple organ

| Model | Variable | β coefficient | p Value | OR (95% CI) |
|--------------------|-------------------|---------------|---------|---------------------|
| Prognostic factors | Basal cistern | 2.862 | 0.001 | 17.49 (3.04–100.73) |
| | Motor response | 2.395 | 0.026 | 10.97 (1.33-90.14) |
| | Intradural lesion | 0.816 | 0.297 | 2.26 (0.48–10.46) |
| | MAP | 1.178 | 0.113 | 3.24 (0.75-13.92) |
| | Midline shift | -0.205 | 0.781 | 0.81 (0.19-3.44) |
| | Constant | -10.282 | 0.001 | , |

dysfunction syndrome) and co-morbidities leading to mistaken conclusions. Further more, sepsis and multiple organ failure (critical illness, systemic inflammatory response syndrome) develop in the majority of patients who received mechanical ventilation for ≥ 1 week in major medical and surgical ICUs. In addition, 1-week mortality data are easily obtained from hospital record, whereas 30-day mortality requires patient follow-up which is burdensome for trauma centers with limited resources. 10,11

There are various predictors for assessing the outcome of head-injured patients. Some of these prognostic factors are discussed below in concurrence with our study.

4.1. Sex and age

Gender differences in the physiological response to TBI are increasingly being described. Although an age threshold has been suggested, current evidence suggest a continuous relationship between increasing age and worsening outcome after TBI. It is believed that this may reflect in decreased capacity for brain repair, as well as increased susceptibility to the complications of TBI. Additionally, some investigations reported better outcomes below the age — of 40–50 years, while other studies reported outcome as a continuous function of age without threshold values. ¹³ Despite the fact that age is a significant factor in predicting mortality, we did not find this factor having correlation in our study (p = 0.139). ^{12–20}

4.2. GCS and motor response

Since its first development in 1974, GCS has become the most frequently used classification of TBI severity. In patients with more severe injuries, the motor component of the GCS has the greatest predictive values because eye and verbal responses are commonly absent in these patients. Marmarou and coauthors reported a stronger association with outcome for an abnormal motor response than for an absent motor

response. In accordance to previous studies, we found that a motoric score >4 showed a more favorable outcome (p=0.026). $^{12-14,16,21}$

4.3. Blood pressure, heart rate, temperature and respiration rate

A single recording of a hypotensive episode is generally associated with a doubled mortality rate and a marked increase in morbidity from a given head injury. Hypotension is one of the few variable that respond to medical manipulation. According to Brain Trauma Guidelines, Class I evidence shows that blood pressure (systolic blood pressure < 90 mmHg), especially in combination with hypoxia, is an indicator of unfavorable outcome. Decrease in blood pressure, MAP and core temperature will cause brain cells ischemia resulting in secondary effect. The Cushing response (arterial hypertension, bradycardia, irregularity in breathing) have important clinical implications, in which the ICP may exhibit some disproportion and usually uncontrollable damage. With a MAP cut off point of 97.17 mmHg, there is a favorable outcome in the survivor group of our study as stated in previous studies. 12,14,17,22–24

4.4. Operation and interval

In severe traumatic brain injury, the condition of patients often worsen gradually within the first 8 h because of the brain ischemia. In this study we did not find any significant correlation between operative management and operation interval. Regardless of this, there was no difference in our study population whether the patient was managed conservatively or undergoing an operation. 12,25

4.5. Head CT scan findings

Prognostic CT findings include; primary CT abnormalities within the first 12 h of TBI, compressed basal cistern at the

| Table 3 $-$ Simplified scoring system of prognostic factors associated with mortality. | | | | | | | |
|--|-----------------------|-------------------------|---------|------------------|-------------|--|--|
| Risk factors | Survived ($n = 21$) | Unsurvived ($n = 40$) | p Value | OR (95% CI) | Sensitivity | | |
| | | | 0.002 | 9.25 (2.14–39.8) | 92.50% | | |
| No major factors | 9 (75.0%) | 3 (25.0%) | | | | | |
| With major Factors | 12 (24.5%) | 37 (75.5%) | | | | | |
| 1 major factor | 11 (28.9%) | 27 (71.1%) | | | | | |
| 2 major factor | 1 (9.1%) | 10 (90.9%) | | | | | |

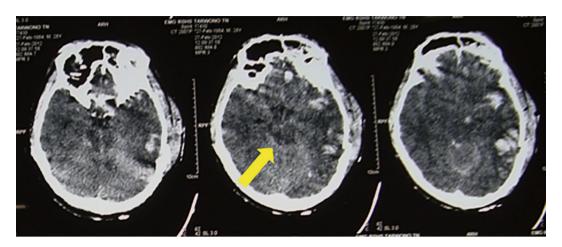


Fig. 1 — A 49-year-old patient with motoric score of 3 and CT findings showing compression of basal cistern (yellow arrow) on midbrain level and multiple cerebral contusion. Even though patient received adequate treatment but he died after 2 days.

level of midbrain, presence of SAH and midline shift. Presence of SAH or intradural lesion and compression of basal cistern are one of the most important criteria in predicting mortality of head-injured patients. As shown on Fig. 1, a head CT scan of one of our patients showing basal cistern compression and multiple cerebral contusion with a grave outcome. In this study, we found compression of basal cistern to be the most dominant variable in determining mortality, in which, it was two or three times higher for cases with compressed or absent cisterns. $^{7,10,22,23,25-31}$

Shifting of midline structures also correlate with outcome even though it is related to other CT signs as well. In the study by Fearnside, et al, ¹⁴ midline shift and other CT parameters were third in correlation strength (after age and motor score) in a logistic regression analysis of the relative importance of prognostic variables. ^{27,30,32–34}

The largest amount of prognostic information was contained in a core set of two predictors: basal cistern compression and poor motoric score. Other variables also had a significant correlation in determining mortality outcomes such as intradural lesions, MAP < 97 mmHg, and midline shift > 5 mm. These characteristics were already considered in the first well-known model for TBI and in many subsequent prognostic models. Whereas in our study, the statistical analysis of age and presence of SAH did not reveal any significant result on mortality, although these two are well known valuable prognostic factors in determining outcome. We believe that this result could be possible due to small sample size in our study. A larger prospective study with a wider range of subjects and variables is needed to provide more information regarding these prognostic factors.

A 92.5% mortality sensitivity is a noteworthy point in patients with both motor response < 4 and absence of basal cistern. We believe that our simple prognostic model can be used as a tool for adequate prognosis information regarding survival chances. Besides -, this model is also advantageous for better clinical decision making, particularly in developing countries such as Indonesia, where adequate health care is still a luxury privilege for most of the population.

5. Conclusions

Although clinicians usually attempt to take a wide range of factors into account when making clinical decisions and assessing prognosis, there is probably, a redundancy in this effort -. Even though there is a little doubt regarding the importance of these features from clinical experiences, there are still debates about the precise nature of their relationships and about exactly how the different features should be assessed, categorized, and—most importantly—utilized. Mortality of severe TBI patients are significantly shown in patients with poor motoric response and compression of basal cisterns. These variables may be useful for providing realistic information to the relatives on expectations of outcome, for quantifying and classifying the severity of brain injury especially for the attending physicians in the emergency department.

Conflicts of interest

All authors have none to declare.

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