THE INDIAN JOURNAL OF NEUROTRAUMA 10 (2013) 3–8

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.elsevier.com/locate/ijnt

Original Article

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

Mardjono Tjahjadi, Muhammad Z. Arifin, Arwinder Singh Gill, Ahmad Faried*

Department of Neurosurgery, Faculty of Medicine, Universitas Padjadjaran, Dr. Hasan Sadikin General Hospital, Jl. Pasteur No 38, Bandung 40161, West Java, Indonesia

ARTICLE INFO

Article history:
Received 13 October 2012
Accepted 10 April 2013
Available online 18 April 2013

Keywords:
Traumatic brain injury
Prognosis
Early mortality

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.

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

* *Corresponding author.*
E-mail address: arwinsingh@hotmail.com (A.S. Gill).

0973-0508/$ – see front matter Copyright © 2013, Neurotrauma Society of India. All rights reserved.
http://dx.doi.org/10.1016/j.ijnt.2013.04.007

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 ≥ 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 ≤ 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 ($p \leq 0.05$). We found mean arterial pressure (MAP > 97.17 mmHg), motor response (≥ 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.

Variables		Survived (n = 21)	Unsurvived (n = 40)	p Value	OR (95%CI)
Patient characteristics					
Sex				0.091	2.75 (0.53–14.14)
	Male	19 (38.0%)	31 (62.0%)		
	Female	2 (18.2%)	9 (81.8%)		
Age				0.139	2.55 (0.72–9.02)
	Average	27.48 (10.56)	36.30 (15.97)		
	<40	17 (40.5%)	25 (59.5%)		
	≥40	4 (21.1%)	15 (78.9%)		
Management				0.61	0.75 (0.24–2.26)
	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)
	<8 h	9 (47.1%)	25 (73.5%)		
	≥8 h	12 (44.4%)	15 (55.60%)		
Physical findings					
MAP				0.027	1.54 (1.01–2.36)
	Average	91.42 (17.48)	100.19 (18.64)		
	≤97.17	13 (50%)	13 (50%)		
	>97.17	8 (22.9%)	27 (77.1%)		
Heart rate				0.596	1.33 (0.46–3.86)
	Average	83.86 (20.44)	88.85 (20.99)		
	≤87.13	12 (37.5%)	20 (62.5%)		
	>87.13	9 (31.0%)	20 (69.0%)		
Respiration rate				0.377	1.67 (0.53–5.20)
	Average	23.86 (5.14)	24.35 (6.05)		
	≤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)		
	≥ 4	19 (59.4%)	13 (40.6%)		
	< 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)
	Compressed	9 (20.5%)	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

Table 2 – Prognostic factors associated with mortality in severe TBI patients.

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	

Multiple Logistic Regression Test.

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.[6] 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%)			

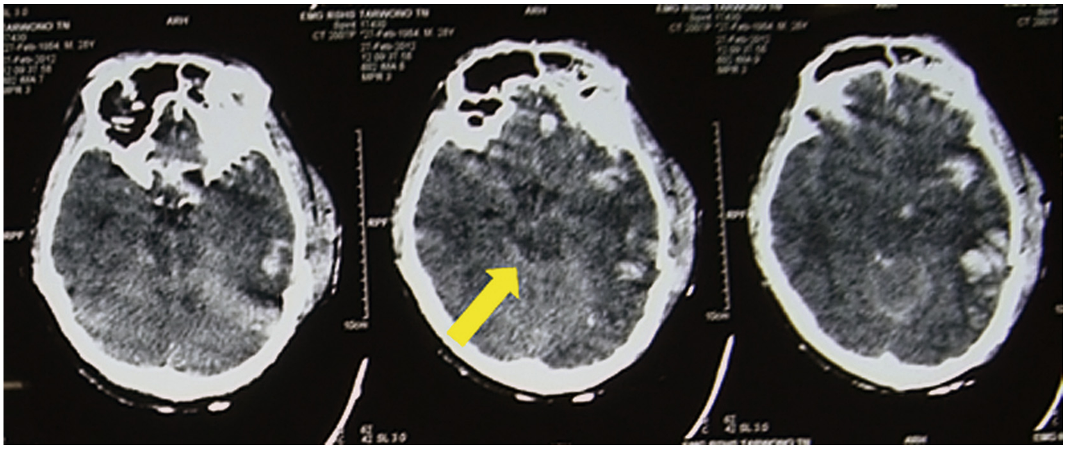

Fig. 1 – A 49-year-old patient with motoric score of 3 and CT findings showing compression of basal cistern (yellow arrow) on midbrain level and multiple cerebral contusion. Even though patient received adequate treatment but he died after 2 days.

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.

REFERENCES

1. Brun Jr J, Hauser WA. The epidemiology of traumatic brain injury: a review. *Epilepsia*. 2003;44:2–10.
2. Bullock R, Chesnut RM, Clifton G, et al. Guidelines for the management of severe head injury. Brain Trauma Foundation. *Eur J Emerg Med*. 1996;3:109–127.
3. Hukkelhoven CW, Steyerberg EW, Habbema JD, et al. Predicting outcome after traumatic brain injury: development and validation of a prognostic score based on admission characteristics. *J Neurotrauma*. 2005;22:1025–1039.
4. Arifin MZ. *tathione Effect on Glutamate Receptor and Cell Death After Traumatic Brain Injury*. Doctorate Dissertation. Department Neurosurg Bandung, Indonesia: Universitas Padjadjaran; 2010.
5. Neurotrauma Team, Dr. Soetomo General Hospital Surabaya. *Traumatic Brain Injury Protocol*. Surabaya, Indonesia: Airlangga University Faculty of Medicine; 2010.

6. Andrews PJ, Sleeman DH, Statham PF, et al. Predicting recovery in patients suffering from traumatic brain injury by using admission variables and physiological data: a comparison between decision tree analysis and logistic regression. *J Neurosurg*. 2002;97:326–336.
7. Hults KN, Marshall LF, Marshall SB. Outcome prediction after severe head injury. In: Reilly PL, Bullock R, eds. *Head Injury Pathophysiology and Management*. 2nd ed. United Kingdom: Hodder Arnold Publishing, UK; 2005:462–471.
8. Signorini DF, Andrews PJ, Jones PA, Wardlaw JM, Miller JD. Predicting survival using simple clinical variables: a case study in traumatic brain injury. *J Neurol Neurosurg Psychiatry*. 1996;66:20–25.
9. Steyerberg EW, Mushkudiani N, Perel P, et al. Predicting Outcome after traumatic brain injury: development and international validation of prognostic scores based on admission characteristics. *PLoS Med*. 2008;5:e165.
10. Bolton CF, Young GB. Managing the nervous system effects of sepsis. *Chest*. 2010;131:1273–1274.
11. Langer M, Cigada M, Mandelli M, Mosconi P, Tognoni G. Early onset pneumonia: a multicenter study in intensive care units. *Intensive Care Med*. 1987;13:342–346.
12. American Association of Neurological Surgery. Guidelines for the management of severe traumatic brain injury. *J Neurotrauma*. 2010;24(suppl 1):S1–S106.
13. Chesnut RM, Ghajar J, Maas AIR, et al. Early indicators of prognosis in severe traumatic brain injury. *J Neurotrauma*. 2000;17:614–619.
14. Fearnside MR, Cook RJ, McDougall P, McNeil RJ. The westmead head injury project outcome in severe head injury. a comparative analysis of prehospital, clinical, and ct variables. *Br J Neurosurg*. 1993;7:267–279.
15. Hukkelhoven CW, Steyerberg EW, Rampen AJ, et al. Patient age and outcome following severe traumatic brain injury: an analysis of 5600 patients. *J Neurosurg*. 2003;99: 666–673.
16. Jennet B. Altered consciousness and coma. In: Crockard A, Hayward R, Hoof JT, eds. *Neurosurgery: The Scientific Basis of Clinical Practice*. 1st ed. UK: Blackwell-Synergy; 1985:117–126. Chapter 26.
17. Puenpathom N, Choomuang M, Ratanalert S. Outcome and outcome prediction in severe head injury. *Surg Neurol*. 1993;40:22–25.
18. Rivas JJ, Lobato RD, Sarabia R, Cordobés F, Cabrera A, Gomez P. Extradural hematoma: analysis of factors influencing the course of 161 patients. *Neurosurgery*. 1988;23:44–51.
19. Temkin NR, Holubkov R, Machamer JE, Winn HR, Dikmen SS. Classification and regression tress (CART) for prediction of function at 1 year following head trauma. *J Neurosurg*. 1995;82:764–771.
20. Vollmer DG, Torner JC, Jane JA, et al. Age and outcome following traumatic comas: why do older patients fare worse? *J Neurosurg*. 1991;75:S37–S49.
21. Boto GR, Gómez PA, De La Cruz J, Lobato RD. Severe head injury and the risk of early death. *J Neurol Neurosurg Psychiatry*. 2006;77:1054–1059.
22. Chesnut RM, Marshall LF, Klauber MR, et al. The role of secondary brain injury in determining outcome from severe head injury. *J Trauma*. 1993;34:216–222.
23. Graham DI. Response of the brain to hypoxia. Chapter 30. In: Crockard A, Hayward R, Hoof JT, eds. *Neurosurgery: The Scientific Basis of Clinical Practice*. 2nd ed. UK: Blackwell-Synergy; 2000:431–447.
24. Lee KR, Hoff JT. Raised intracranial pressure and its effect on brain function. In: Crockard A, Hayward R, Hoof JT, eds. *Neurosurgery: The Scientific Basis of Clinical Practice*. 2nd ed. UK: Blackwell-Synergy; 2000:393–407. Chapter 28.
25. Wilberger Jr JE, Harris M, Diamond DL. Acute subdural hematoma: morbidity. Mortality, and operative timing. *J Neurosurg*. 1991;74:212–218.
26. Athiappan S, Muthukumar N, Srinivasan US. Influence of basal cistern, midline shift, and pathology on outcome in head injury. *Ann Acad Med Singapore*. 1993;22:452–455.
27. Eisenberg HM, Gary Jr HE, Aldrich EF, et al. Initial ct findings in 753 patients with severe head injury. A report from the NIH traumatic coma data bank. *J Neurosurg*. 1990;73:688–698.
28. Greene KA, Marciano FF, Johnson BA, Jacobowitz R, Spetzler RF, Harrington TR. Impact of traumatic subarachnoid hemorrhage on outcome in non-penetrating head injury. Part I: a computerized tomography grading scale. *J Neurosurg*. 1995;83:445–452.
29. Marshall LF, Marshall BS, Klauber MR, et al. A new classification of head injury based on computed tomography. *J Neurosurg*. 1991;75:S14–S20.
30. Jun-ichi Ono, Yamaura A, Kubota M, et al. Early prediction of an outcome in severe head injury: result of analyses of the glasgow coma scale score, the patient's age, and the CT findings. *Jpn J Neurosurg*. 1996;5:133–141.
31. Taneda M, Kataoka K, Akai F, Asai T, Sakata I. Traumatic subarachnoid hemorrhage as a predictable indicator of delayed ischemic symptoms. *J Neurosurg*. 1996;84:762–768.
32. Kotwica Z, Brzeziński J. Acute subdural hematoma in adults. An analysis of outcome in comatose patients. *Acta Neurochir (Wien)*. 1993;121:95–99.
33. Selladurai BM, Jayakumar R, Tan YY, Low HC. Outcome prediction in early management of severe head injury. *Br J Neurosurg*. 1992;6:549–557.
34. Zumkeller M, Behrmann R, Heissler HE, Dietz H. Computed tomographic criteria and survival rate for patients with acute subdural hematoma. *Neurosurgery*. 1996;39:708–712.