Prognostic factors for mortality in patients with severe traumatic brain injury in Yogyakarta, Indonesia

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ABSTRACTS

Determining an accurate prognosis in patients with severe traumatic brain injury (TBI) still becomes a difficult challenge for neurologists. Clinical and laboratory findings have been used as important parameters to establish clinical decisions or even predict future prognosis including death in these patients. We studied the clinical, laboratory and neuroimaging parameters in predicting mortality in patients with severe TBI. This study used the medical records of severe TBI cases in Dr. Sardjito General Hospital, Yogyakarta, Indonesia from January 2015 until July 2016. We evaluated the clinical, laboratory, and neuroimaging examinations of seventy patients with severe TBI in association with mortality. The result showed among 70 patients involved, 35 were dead. Clinical findings of age <40 y.o. (OR=1.143; p=0.015), multiple injuries (OR=5.712; p=0.045), and systolic blood pressure >140 mmHg (OR=3.852; p=0.008) were associated with mortality. Laboratory and neuroimaging parameters of hyponatremia (OR=3.667; p=0.027), hyperkalemia (OR=1.771; p=0.030), and the presence of traumatic subarachnoid hemorrhage (SAH) (OR=6.526; p=0.003) in head CT-scan were significantly associated with mortality. In conclusion, our study showed that productive age <40 y.o. multiple injuries, hyponatremia, hyperkalemia and the presence of traumatic SAH increase the mortality risk in patients with severe TBI.

ABSTRAK

Menentukan prognosis yang akurat pada pasien dengan traumatic brain injury (TBI) parah masih menjadi tantangan berat bagi spesialis saraf. Temuan klinis dan laboratorium telah digunakan sebagai parameter penting untuk menetapkan keputusan klinis atau bahkan memprediksi prognonsinya termasuk kematian pada pasien ini. Kami mempelajari parameter klinis, laboratorium dan neuroimaging untuk memprediksi kematian pada pasien dengan TBI parah. Penelitian menggunakan rekam medis kasus TBI parah di Rumah Sakit Umum Pusat Dr. Sardjito, Yogyakarta, Indonesia dari Januari 2015 hingga Juli 2016. Kami mengevaluasi pemeriksaan klinis, laboratorium, dan neuroimaging dari 70 pasien dengan TBI parah terkait dengan kematian. Diantara 70 pasien yang terlibat, 35 meninggal. Usia <40 tahun (OR = 1,143; p = 0,015), beberapa cedera (OR = 5,712; p = 0,045), dan tekanan darah sistolik > 140 mmHg (OR = 3,852; p = 0,008) dikaikan dengan kematian. Parameter laboratorium dan neuroimaging hiponatremia (OR = 3,667; p = 0,027), hyperkalemia (OR = 1,771; p = 0,030) dan adanya subarachnoid hemorrhage (SAH) trauma (OR = 6,526; p = 0,003) pada CT-scan kepal terkait nyata dengan kematian. Dapat disimpulkan dari penelitian ini, usia produktif <40 tahun, beberapa cedera, hiponatremia, hyperkalemia dan adanya SAH trauma meningkatkan risiko kematian pada pasien dengan TBI parah.

Keywords: severe traumatic brain injury; subarachnoid hemorrhage; increased blood pressure; hyponatremia; hyperkalemia; mortality;
INTRODUCTION

Nearly 80% of all fatal trauma are accompanied with a traumatic brain injury (TBI). Traumatic brain injury affected almost 1.5 million people in the United States each year and 240,000 required hospitalization for treatment of their trauma. Of the total, 60,000 people died and 70,000 people were suffered from permanent neurological disabilities. In 2005, there were 434 with mild head injury, 315 patients with moderate head injury, and 28 patients with severe head injury who were hospitalized in Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia. In contrast, there were 347 cases of head injuries in Siloam Gleneagles Private Hospital overall. Traumatic brain injury is a clinically heterogeneous condition of causes, pathology, severity, prognosis and also outcomes.

Traumatic brain injury can be divided into primary and secondary TBI according to its pathophysiology. Primary TBI is resulted from the initial mechanical strength of the trauma leading to physical damage of cell membranes and infrastructure, disruption of homeostasis and increased permeability of the membrane. These in turn can lead to astrocytic and neuronal swelling, relative hypoperfusion and neurotoxicity. Secondary TBI is described as further physiological consequences, such as ischemia, reperfusion disorders and hypoxia, that cause brain lesions in the future. Secondary TBI is influenced by various factors such as hypoperfusion in the cerebral blood flow, impaired cerebrovascular autoregulation and CO$_2$-reactivity, cerebral vasospasm and metabolic dysfunction of the brain. As a result, brain oxygenation can not be fulfilled.

Intracranial and extracranial factors causing secondary TBI are the main targets for medical interventions to prevent brain damage. Several methods have been reported to monitor the causes of secondary TBI in order to ensure better outcomes in patients with TBI. Due to the variety of clinical findings in TBI patients, determining the prognosis in patients with TBI is often difficult. Hence, an accurate prognosis is very important for clinical decision making. In fact, it is almost impossible to determine the patient's prognosis immediately after a TBI due to the limited initial clinical assessments, variations in the recovery duration, as well as other factors.

Identification of the factors that can be used as predictors of outcome of patients with head injuries is important not only for clinical decision making but also education to the patient or his family. One of the laboratory parameters that is often examined in patients with TBI is arterial blood gas analysis (ABG). The ABG is an examination that can provide an overview of acid-base balance and provide the needs and requirements of oxygen in the brain. In some studies, the levels of arterial blood PCO$_2$ on admission or time of hospital admission can be used as predictors of outcome in patients with TBI. Moreover, the oxygenation and ventilation on hospital admission was not significantly related to the outcome of patients with severe TBI.

In this study, we evaluated several clinical, laboratory and neuroimaging parameters that are associated with mortality in patients with severe TBI. The significant parameters in our study might be suggested as useful indicators in predicting the prognosis of patients with severe TBI.

MATERIALS AND METHODS

Subjects

This was a case control study that aimed to determine the clinical, laboratory and neuroimaging parameters in predicting mortality.
of severe TBI patients in Dr. Sardjito General Hospital, Yogyakarta, Indonesia. We reviewed the data of patients with severe TBI from the Medical Record Unit of Dr. Sardjito General Hospital. Samples in this study were all severe TBI patients treated at Dr. Sardjito General Hospital, Yogyakarta, Indonesia and met the inclusion and exclusion criteria.

Protocol of study

Severe TBI patients were defined as trauma patients with Glasgow coma score (GCS) of 3 – 8 or proven intracranial hemorrhage in neuroimaging. The study sample was patients with severe TBI treated at Dr. Sardjito General Hospital, Yogyakarta, Indonesia who were hospitalized between January 2015 until July 2016. The exclusion criteria include patients with chronic kidney disease (CKD) and patients with chronic obstructive pulmonary disease (COPD). Baseline characteristics, clinical findings, laboratory parameters and neuroimaging results data of patients were collected. This study has been approved by the Medical and Health Research Ethics Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta (Ref. KE/FK/1168/EC/2017).

Statistical analysis

The quantitative data were presented as mean ± standard deviation (SD). A Chi-square test was used to evaluate the relationship between categorical variables and mortality. Demographic characteristics, clinical and laboratory parameters on admission with a p-value < 0.20 were included in the final backward stepwise regression model. The backward stepwise logistic regression model was used to estimate the odds ratios (OR) for final analysis after adjustment for potential confounding factors. All statistical tests of significance were two-tailed, and p<0.05 was considered as significant.

RESULTS

A total 70 severe TBI patients were included in this study with baseline characteristics are shown in TABLE 1. Most of the patients with severe TBI were male, in the range of productive age (<50 y.o.), and arrived at the hospital less than 8 h after the trauma occurred.

| Variables          | Mean ± SD | n  | % |
|--------------------|-----------|----|----|
| Gender             |           |    |    |
| • Male             | 50        | 50 | 71.4 |
| • Female           | 20        | 20 | 28.6 |
| Age                | 45.86 ± 17.518 | 70 |    |
| • <40              | 18        | 18 | 25.7 |
| • >50              | 30        | 30 | 42.8 |
| • 40-50            | 22        | 22 | 31.4 |
| Multiple trauma    |           |    |    |
| • Yes              | 11        | 11 | 15.7 |
| • No               | 59        | 59 | 84.3 |
| Arrival            | 12.68 ± 9.847 | 70 |    |
| • <8 hours         | 34        | 34 | 48.6 |
| • >24 hours        | 11        | 11 | 15.7 |
| Variables                                   | Mean ± SD     | n  | %  |
|---------------------------------------------|---------------|----|----|
| • 8-24 hours                                | 25            | 35  | 70  |
| Surgery                                     |               |    |    |
| • Yes                                       | 47            | 67  | 134 |
| • No                                        | 23            | 33  | 67  |
| Head CT scan result                         |               |    |    |
| • SDH                                       | 29            | 41  | 166 |
| • SAH                                       | 20            | 28  | 56  |
| • EDH                                       | 35            | 50  | 112 |
| Systolic blood pressure                     | 139.41 ± 25.315 | 29 | 41  |
| • >=140                                     |               | 41  | 77  |
| Dyastolic blood pressure                    | 81.72 ± 12.341 | 16 | 22  |
| • >=90                                      |               | 54  | 77  |
| Pulse                                       |               |    |    |
| • <60                                       | 6             | 8.6 | 10  |
| • >100                                      | 10            | 14.3 | 14.3 |
| • 60-100                                    | 54            | 77  | 134 |
| Respirationrate                             | 20.52 ± 3.202 | 1  | 1.4 |
| • <12                                       |               | 20  | 28.6 |
| • >20                                       |               | 49  | 70  |
| Temperature                                 | 36.70 ± 2.328 | 7  | 10  |
| • <36.5                                     |               | 4   | 5.7 |
| • >37.5                                     |               | 59  | 84.3 |
| Hb                                          |               | 48  | 68.6|
| • <12                                       |               | 22  | 31.4|
| • 12-17                                     |               | 22  | 31.4|
| • Leukocyte                                 | 14063.60 ± 11247.37 | 4  | 5.7 |
| • <4000                                     |               | 48  | 68.6|
| • >10000                                    |               | 18  | 25.7|
| • 4000-10000                                |               | 18  | 25.7|
| Platelets                                   | 221.18 ± 132.893 | 7  | 10  |
| • <150000                                   |               | 4   | 5.7 |
| • >400000                                   |               | 59  | 84.3|
| • 150000-40000                              |               | 59  | 84.3|
| Natrium                                     | 141.46 ± 8.90 | 14  | 20.0|
| • <135                                      |               | 24  | 34.3|
| • >145                                      |               | 32  | 45.7|
| Potassium                                   | 3.70 ± 0.66   | 22  | 31.4|
| • <3.5                                      |               | 7   | 10.0|
| • >4.5                                      |               | 41  | 58.6|
| • 3.5-4.5                                   |               | 41  | 58.6|
In this study, patients whose age were <40 y.o. were associated with mortality (TABLE 2). In clinical parameters, during secondary survey, only 15.7% patients with severe TBI were suffered from multiple traumas (TABLE 1). However, multiple traumas in patients with severe TBI were associated with mortality (TABLE 2).

### TABLE 2. Bivariate analysis of characteristics, laboratory finding to mortality of severe TBI patients

| Variables                  | n (%) | Died [n (%)] | Survived [n (%)] | OR   | 95% CI | p      |
|----------------------------|-------|--------------|------------------|------|--------|--------|
| Gender                     |       |              |                  |      |        |        |
| • Male                     | 50 (71.4) | 24 (48.0) | 26 (52.0) | 0.755 | 0.267-2.139 | 0.597 |
| • Female                   | 20 (28.6) | 11 (55.0) | 9 (45.0)   |      |        |        |
| Age                        |       |              |                  |      |        |        |
| • <40                      | 18 (25.7) | 6 (33.3)   | 12 (66.7)   | 1.143 | 0.309-4.234 | 0.015 |
| • >50                      | 30 (42.8) | 21 (70.0)  | 9 (30.0)   | 0.245 | 0.076-0.788 | 0.184 |
| • 40-50                    | 22 (31.4) | 8 (36.4)   | 14 (63.6)  |      |        |        |
| Multiple injuries          |       |              |                  |      |        |        |
| • Yes                      | 11 (15.7) | 9 (81.8)   | 2 (18.2)   | 5.712 | 1.135-28.748 | 0.045 |
| • No                       | 59 (84.3) | 26 (44.1)  | 33 (55.9)  |      |        |        |
| Arrival                    |       |              |                  |      |        |        |
| • <8 hours                 | 34 (48.6) | 17 (50.0)  | 17 (50.0)  | 0.923 | 0.328-2.594 | 0.937 |
| • >24 hours                | 11 (15.7) | 6 (54.5)   | 5 (45.5)   | 0.769 | 0.185-3.191 | 0.808 |
| • 8-24 hours               | 25 (35.7) | 12 (48)    | 13 (52)    |      |        |        |
| Surgery                    |       |              |                  |      |        |        |
| • Yes                      | 47 (67.1) | 16 (34.0)  | 31 (66.0)  | 0.109 | 0.032-0.374 | 0.000 |
| • No                       | 23 (32.9) | 19 (82.6)  | 4 (17.4)   |      |        |        |
| SDH                        |       |              |                  |      |        |        |
| • Yes                      | 29 (41.4) | 14 (48.3)  | 15 (51.7)  | 0.889 | 0.343-2.302 | 0.808 |
| • No                       | 41 (58.6) | 21 (51.2)  | 20 (48.8)  |      |        |        |
| SAH                        |       |              |                  |      |        |        |
| • Yes                      | 20 (28.6) | 16 (45.7)  | 4 (11.4)   | 6.526 | 1.897-22.452 | 0.003 |
| • No                       | 50 (71.4) | 19 (38)    | 31 (62)    |      |        |        |
| EDH                        |       |              |                  |      |        |        |
| • Yes                      | 35 (50.0) | 12 (34.3)  | 23 (65.7)  | 0.272 | 0.101-0.730 | 0.009 |
| • No                       | 35 (50.0) | 23 (65.7)  | 12 (34.3)  |      |        |        |
| Variables          | n (%) | Died [n (%)] | Survived [n (%)] | OR     | 95% CI       | p    |
|--------------------|-------|--------------|------------------|--------|--------------|------|
| **SBP**            |       |              |                  |        |              |      |
| ≥140               | 29 (41.4) | 20 (69.0) | 9 (31.0) | 3.852 | 1.401-10.590 | 0.008 |
| <140               | 41 (58.6) | 15 (36.6)  | 26 (63.4) |        |              |      |
| **DBP**            |       |              |                  |        |              |      |
| ≥90                | 16 (22.9) | 9 (56.3)  | 7 (43.8) | 1.385 | 0.451-4.255 | 0.569 |
| <90                | 54 (77.1) | 26 (48.1) | 28 (51.9) |        |              |      |
| **Pulse**          |       |              |                  |        |              |      |
| <60                | 6 (8.6%) | 3 (50.0)   | 3 (50.0) | 0.929 | 0.172-5.017  | 0.789 |
| >100               | 10 (14.3) | 6 (60.0)  | 4 (40.0) | 0.619 | 0.157-2.444  |      |
| 60-100             | 54 (77.1) | 26 (48.1) | 28 (51.9) |        |              |      |
| **Respirationrate**|       |              |                  |        |              |      |
| <12                | 1 (1.4%) | 1 (100)    | 0 (0) | 0.000 | 0.000-       | 0.315 |
| >20                | 20 (28.6) | 12 (60.0) | 8 (40.0) | 0.543 | 0.189-1.563  |      |
| 14-20              | 49 (70.0) | 22 (44.9) | 27 (55.1) |        |              |      |
| **Temperature**    |       |              |                  |        |              |      |
| <36.5              | 7 (10.0) | 3 (42.9)   | 4 (57.1) | 1.204 | 0.248-5.857  | 0.117 |
| >37.5              | 4 (5.7) | 4 (100)    | 0 (0) | 0.000 | 0.000-       |      |
| 36.5-37.5          | 59 (84.3) | 28 (47.5) | 31 (52.5) |        |              |      |
| **Hb**             |       |              |                  |        |              |      |
| <12                | 48 (68.6) | 25 (52.1) | 23 (47.9) | 1.304 | 0.474-3.590  | 0.607 |
| 12-17              | 22 (31.4) | 10 (45.5) | 12 (54.5) |        |              |      |
| **Leukocytes**     |       |              |                  |        |              |      |
| <4000              | 4 (5.7) | 2 (50)     | 2 (50) | 0.636 | 0.072-5.613  | 0.543 |
| >10000             | 48 (68.6) | 26 (54.2) | 22 (45.8) | 0.538 | 0.178-1.625  |      |
| 4000-10000         | 18 (25.7) | 7 (38.9)  | 11 (61.1) |        |              |      |
| **Platelets**      |       |              |                  |        |              |      |
| <150000            | 7 (10.0) | 3 (42.9)   | 4 (57.1) | 1.204 | 0.248-5.857  | 0.117 |
| >40000000         | 4 (5.7) | 4 (100)    | 0 (0) | 0.000 | 0.000-       |      |
| 1500000-40000000   | 59 (84.3) | 28 (47.5) | 31 (52.5) |        |              |      |
| **Natrium**        |       |              |                  |        |              |      |
| <135               | 14 (20.0) | 3 (21.4)  | 11 (78.6) | 3.667 | 0.858-15.671 | 0.027 |
| >145               | 24 (34.3) | 16 (66.7) | 8 (33.3) | 0.500 | 0.167-1.496  |      |
| 135-145            | 32 (45.7) | 16 (50)   | 16 (50) |        |              |      |
| **Kalium**         |       |              |                  |        |              |      |
| <3.5               | 22 (31.4) | 16 (72.7) | 6 (27.3) | 0.266 | 0.086-0.818  | 0.030 |
| >4.5               | 7 (10.0) | 2 (28.6)  | 5 (71.4) | 1.771 | 0.307-10.227 |      |
| 3.5-4.5            | 41 (58.6) | 17 (41.5) | 24 (58.5) |        |              |      |
| **Chloride**       |       |              |                  |        |              |      |
| <95                | 3 (4.3) | 3 (100)    | 0 (0) | 0.000 | 0.000-       | 0.039 |
| >105               | 45 (64.3) | 25 (55.6) | 20 (44.4) | 0.373 | 0.128-1.091  |      |
| 95-105             | 22 (31.4) | 7 (31.8)  | 15 (68.2) |        |              |      |
| **Albumin**        |       |              |                  |        |              |      |
| <3.5               | 42 (60.0) | 23 (54.8) | 19 (45.2) | 1.614 | 0.615-4.233  | 0.329 |
| Normal             | 28 (40.0) | 12 (42.9) | 16 (57.1) |        |              |      |
| Variables       | n (%) | Died [n (%)] | Survived [n (%)] | OR   | 95% CI       | p      |
|-----------------|-------|--------------|------------------|------|--------------|--------|
| **pH**          |       |              |                  |      |              |        |
| <7.35           | 20 (28.6) | 11 (55.0) | 9 (45.0) | 0.701 | 0.237-2.071 | 0.771  |
| >7.45           | 11 (15.7) | 6 (54.5)  | 5 (45.5) | 0.714 | 0.186-2.737 |        |
| 7.35-7.45       | 39 (55.7) | 18 (46.2) | 21 (53.8) |      |              |        |
| **pO₂**         |       |              |                  |      |              |        |
| <80             | 9 (12.9)  | 6 (66.7)  | 3 (33.3) | 2.207 | 0.505-9.639 | 0.477  |
| Normal          | 61 (87.1) | 29 (47.5) | 32 (52.5) |      |              |        |
| **pCO₂**        |       |              |                  |      |              |        |
| <35             | 29 (41.4) | 15 (51.7) | 14 (48.3) | 1.200 | 0.437-3.292 | 0.191  |
| >45             | 9 (12.9)  | 2 (22.2)  | 7 (77.8)  | 4.500 | 0.806-25.122|        |
| Normal          | 32 (45.7) | 18 (56.3) | 14 (43.8) |      |              |        |
| **HCO₃⁻**       |       |              |                  |      |              |        |
| <22             | 32 (45.7) | 21 (65.6) | 11 (34.4) | 0.320 | 0.112-0.911 | 0.053  |
| >26             | 9 (12.9)  | 3 (33.3)  | 6 (66.7)  | 1.222 | 0.253-5.909 |        |
| 22-26           | 29 (41.4) | 11 (37.9) | 18 (62.1) |      |              |        |
| **Metabolic acidoses** |       |              |                  |      |              |        |
| Yes             | 13 (18.6) | 9 (69.2)  | 4 (30.8)  | 2.683 | 0.740-9.726 | 0.218  |
| No              | 57 (81.4) | 26 (45.6) | 31 (54.4) |      |              |        |
| **Metabolic alcaloses** |      |              |                  |      |              |        |
| Yes             | 2 (2.9)   | 0 (0)     | 2 (100)   | 2.061 | 1.613-2.632 | 0.493  |
| No              | 68 (97.1) | 35 (51.5) | 33 (48.5) |      |              |        |
| **Respiratory acidoses** |      |              |                  |      |              |        |
| Yes             | 6 (8.6)   | 1 (16.7)  | 5 (83.3)  | 0.176 | 0.020-1.597 | 0.198  |
| No              | 64 (91.4) | 34 (53.1) | 30 (46.9) |      |              |        |
| **Respiratory alcaloses** |      |              |                  |      |              |        |
| Yes             | 6 (8.6)   | 4 (66.7)  | 2 (33.3)  | 2.129 | 0.364-12.459| 0.673  |
| No              | 64 (91.4) | 31 (48.4) | 33 (51.6) |      |              |        |
| **Normal ABG**  |       |              |                  |      |              |        |
| Yes             | 43 (61.4) | 21 (48.8) | 22 (51.2) | 0.886 | 0.338-2.322 | 0.806  |
| No              | 27 (38.6) | 14 (51.9) | 13 (48.1) |      |              |        |

Note: SDH: subdural hematoma; SAH: subarachnoid hemorrhage; EDH: epidural hematoma; SBP: systolic blood pressure; DBP: diastolic blood pressure; Hb: hemoglobin; pO₂: partial pressure of oxygen; pCO₂: partial pressure of carbon dioxide; ABG: arterial blood gas; OR: odd ratio; 95% CI: 95% confidence interval; p: probability

Systolic blood pressure (SBP) was also found to be useful in predicting mortality in severe TBI patients. Increased SBP of >140 mmHg in these patients was significantly associated with mortality (Table 3). Our findings showed that other clinical parameters in vital signs, such as body temperature, respiration rate, pulse rate, and diastolic blood pressure (DBP), were not significantly correlated with mortality (Table 2).

Hyponatremia and hyperkalemia were significant laboratory parameters associated with mortality in severe TBI patients (Table 2). We did not find any other significant laboratory parameters that were significant in predicting mortality in severe TBI patients. Even an immediate ABG, a laboratory parameter to evaluate patient’s oxygenation, did
not show prognostic value in predicting mortality (TABLE 2). More than 60% of patients with severe TBI in our study showed normal interpretation of ABG (TABLE 3). The most frequent abnormal ABG in our severe TBI patients was metabolic acidosis (TABLE 3). Individual parameter of ABG, such as levels of pH, pCO$_2$, pO$_2$, HCO$_3$, and PaO$_2$/FiO$_2$ ratio, also did not show any significant association with mortality (TABLE 3).

### TABLE 3. Interpretation of arterial blood gas analysis

| Types of ABG interpretation | n  | %    |
|-----------------------------|----|------|
| Respiratory acidosis        | 6  | 8.6  |
| Metabolic acidosis          | 13 | 18.6 |
| Respiratory alkalosis       | 6  | 8.6  |
| Metabolic alkalosis         | 2  | 2.9  |
| Normal ABG                  | 43 | 61.4 |

Note: ABG: arterial blood gas

From neuroimaging studies, all 70 patients showed intracranial bleeding with 14 patients showed multiple hemorrhages, for example SAH accompanied with subdural hemorrhage (SDH). Patients whose neuroimaging study showed SAH or epidural hemorrhage (EDH) showed significant association with mortality (TABLE 2). Due to the severity and the natural course of the disease, even surgery could be associated with mortality of these patients (TABLE 2).

Of all the significant parameters mentioned above as predicting factors for mortality in patients with severe TBI, multiple trauma (OR:8.833; 95%CI:1.119 - 69.741), increased systolic blood pressure (OR:5.162; 95%CI:1.303 - 20.440) and SAH finding in neuroimaging study (OR:5.897; 95%CI:1.238 - 28.097) were statistically significant as prognostic factors of mortality in patients with severe TBI (TABLE 4).

### TABLE 4. Multivariate analysis

| Variables         | Exp (B) | OR     | 95%CI          | p   |
|-------------------|---------|--------|----------------|-----|
| SBP               | 1.641   | 5.162  | 1.303-20.440   | 0.019|
| SAH               | 1.774   | 5.897  | 1.238-28.097   | 0.026|
| Multiple trauma   | 2.178   | 8.833  | 1.119-69.741   | 0.039|

Note: SBP: systolic blood pressure; SAH: subarachnoid hemorrhage; OR: odd ratio; 95%CI: 95% confidence interval; p: probability
DISCUSSION

Head trauma and risk factors of mortality after TBI in adults have been studied extensively over the past five decades. Traumatic brain injury is a common cause of morbidity and mortality in people of all ages. Following the acute mechanical insult, TBI evolves over time comprising seconds to days. Understanding the secondary factors that contribute to TBI might suggest therapeutic strategies to reduce the long-term consequences of brain trauma.

In this study, we found that patients whose age were <40 y.o., were suffered from multiple trauma, had increased SBP, hyponatremia, hyperkalemia, showed SAH and EDH were associated with mortality. The ABG as interpreted results or as individual variables including levels of pH, pCO\(_2\), pO\(_2\), HCO\(_3\), and PaO\(_2\)/FiO\(_2\) ratio had no significant relationship with death in these TBI cases.

Of the clinical parameters, severe TBI patients whose age <40 y.o. and who were suffered from multiple injuries showed significant increase in mortality. This might be due to the nature of the accidents that involved higher velocity in relatively younger age (productive age). As a result, the impacts may produce severe multiple injuries. Combining these two factors, people at younger age who were suffered from severe TBI may have tendency in the increase of mortality rate.

Hyponatremia and hypercalcemia may worsen the metabolic state in severe TBI patients. Therefore, electrolyte imbalance in trauma patients should be corrected accordingly to reduce the potential factors for mortality. Regarding ABG, our finding is in contrast with previous study from Bardt et al.\(^{20}\) that reported association of cerebral hypoxia with poor neurological outcome, identifying monitoring of pO\(_2\) as asignificant independent parameter in patients following TBI. Stiefel et al.\(^{16}\) stated that the use of both ICP and brain tissue pO\(_2\) monitors and therapy directed at brain tissue pO\(_2\) is associated with reduced patient death following severe TBI. Bard et al.\(^{20}\) also showed that cerebral hypoxia have association with poor neurological out come in TBI patients. Van Santbrink et al.\(^{21}\) reported that disturbances of the oxygen regulation after TBI is a prognostic value and may aid in identifying patients at risk for ischemia.

From the neuroimaging studies, patients who had EDH and SAH showed significant increase in mortality. This is due to the nature of EDH and SAH that may worsen anytime. The delay in seeking for medical assistance and proper management in intracranial hemorrhage may lead to an undesirable outcome, including death. Therefore, all head trauma should be treated as an emergency as for intracranial hemorrhage, until proven otherwise.

These findings were affected by several factors. One of them is probably related to the fact that Dr. Sardjito General Hospital, Yogyakara is a referral hospital. Therefore, the patients were likely to have received resuscitation or oxygen therapy in the previous hospitals or en route to the hospital using ambulance. This is supported by our data that showed less abnormal ABG compared to normal ABG in patients with severe TBI. This finding is in accordance with previous study by Jousi et al.\(^{22}\) which showed pre-hospital use of small-volume resuscitation led to significantly greater decrease of BE and pH values.

CONCLUSION

In conclusion, productive age of <40 y.o., multiple injuries, hyponatremia, hyperkalemia and the presence of SAH increase the mortality risk in patients with severe TBI.
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