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ANALYSIS OF FACTORS CAUSING DETERIORATION IN PATIENTS WITH HEAD TRAUMA

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ABSTRACT
The incidence of head trauma continues to increase from year to year and causes death or disability in adults. Factors that cause deterioration in patients with head trauma are age, initial Glasgow Coma Scale (GCS), RTS (Revised Trauma Score), blood pressure, travel time to hospital (RS), and other organ trauma. Deterioration in head trauma patients can be seen from the Glasgow Outcome Scale (GOS). The problem formulation in this study is how the factors that cause deterioration in patients with head trauma are related. The purpose of this study is to describe the relationship between factors that cause deterioration in patients with head trauma and find the dominant factor. This research method is comparative analytic with a cross-sectional design. Respondents were selected using purposive sampling with a total of 48 respondents. Data on GOS, age, GCS, RTS, and blood pressure were collected from patient medical records. Data on travel time to hospital were collected from interviews with patients' families. The obtained data were subjected to multivariate analysis using logistic regression tests. The results showed that the variables of age, GCS, RTC, blood pressure, and travel time to hospital have a relationship with the GOS variable (p-value <0.005). The results of a multivariate logistic regression analysis showed that the most dominant factor influencing the worsening of severe head injury (GOS) was the RTC value (OR:16.18). In conclusion, a lower RTC value indicates a worse prognosis for head injury patients.

Keywords: glasgow outcome scale; head trauma; revised trauma score

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INTRODUCTION

The incidence of head trauma continues to increase from year to year and causes death or disability in adults and children. Head trauma is trauma to the head that includes the skull and cerebral/brain bones. Head trauma can occur due to impact with a solid object with an acceleration and/or deceleration trauma mechanism. Individuals who experience head trauma are usually caused by traffic accidents, falls, or fights. Head trauma can cause bleeding in the brain, cerebral edema, neurological disorders, decreased consciousness, and increased intracranial pressure. The classification of head trauma is determined by the GCS (Glasgow Coma Scale) score. Mild head trauma has a GCS score of 14-15, moderate head trauma has a GCS score of 9-13, and severe head trauma has a GCS score of less than 8. The incidence rate / epidemiological results, an estimated 10% of patients with head trauma experience death before being taken to the hospital's Emergency Room (ER). Estimated incidence rates/epidemiological results of each classification of head trauma are: severe head trauma 10%, moderate head trauma 10%, and severe head trauma 80% (Rizkiya, P., et al. 2020)

Head trauma or traumatic brain injury is defined as trauma to the head due to blunt trauma or penetrating trauma or acceleration and deceleration forces that cause temporary or permanent brain dysfunction. Some experts use the term craniocerebral trauma based on the understanding that the injury or lesion that occurs can affect the skull (cranium) or brain tissue (cerebral) or both at once (Putri, T. I., et al. 2021). Head trauma is a deformation in the form of deviation in shape or deviation in the line of the bone or skull shaft, where acceleration and deceleration are changes in shape that are influenced by changes in increasing and decreasing speed factors. Meanwhile, according to the opinion of Head Trauma is a forced injury (trauma) that affects the head structure so that it can cause structural abnormalities and/or functional disorders in brain tissue. The resulting disorders can be temporary or permanent, such as cognitive, psychological, intellectual deficits, and trauma disorders caused by head trauma can affect various components of both the external and internal brain components, including the skull and brain. Several definitions above can be concluded that head trauma is trauma to the scalp, skull, and brain either directly or indirectly to the head that results in decreased consciousness or death. (Adeleye, A.O. & Ogun, M.I. 2017)

Acceleration is a mechanism of head trauma that occurs when a moving object strikes a stationary head, while deceleration occurs when a moving head strikes a stationary object. Head trauma will cause disorders that are complex in nature compared to other trauma. This is due to the anatomical and physiological nature of the contents and spaces of the skull that are complex with liquid, soft, and solid consistency, namely cerebrospinal fluid, meninges, nerve tissue, blood vessels and bone. The outcome of head trauma is determined by two different mechanisms: a). Primary insult (primary damage, mechanical damage) that occurs at the time of impact, b). Secondary insult (secondary damage, delayed nonmechanical damage) shows a sequential pathological process that begins at the time of trauma with a delayed clinical presentation. Cerebral ischemia and intracranial hypertension are included in secondary insults (Husnah, K., at al. 2019).

Cerebral blood flow is maintained at a constant level in the normal brain during normal fluctuations in blood pressure by a process called autoregulation. This autoregulation maintains a constant blood flow between a mean arterial pressure (MAP) of 50 mmHg and 150 mmHg. However, in an ischemic or traumatized brain, or in the presence of vasodilators (such as vasodilators and sodium nitroprusside), cerebral blood flow (CBF) can be dependent on blood pressure. Defects in cerebral blood flow autoregulation may appear immediately after trauma or may develop over time, and may be transient or persistent in circumstances that reflect mild, moderate, or severe damage. Thus, when arterial pressure increases, CBF increases, leading to an increase in brain volume. Similarly, when pressure decreases, CBF decreases, reducing intracranial pressure but also triggering an uncontrolled reduction in CBF. Cerebrovascular autoregulation and CO2 reactivity are important mechanisms for ensuring adequate cerebral blood flow at all times. Likewise, both patterns are fundamental to the management of cerebral perfusion pressure and intracranial pressure, and impaired regulatory mechanisms reflect an increased risk of secondary brain damage. Impaired consciousness is a frequent symptom of brain trauma. The fluctuating level of consciousness and its duration are important indicators of the progress or decline of a patient's condition with brain trauma. A progressively decreased level of consciousness indicates a worsening condition. A decrease in the GCS score of 2 or more indicates significant deterioration and should be reported immediately to the treating physician (Kurowski, B. G., et al. 2024)

Head trauma causes increased intracranial pressure. Pressure is the ratio between cross-sectional area and volume. In this case, the cross-sectional area is the cranial bones, and the volume is the contents within the cranium. Increasing cranial components will result in increased intracranial pressure. Increased brain volume in head trauma occurs due to bleeding and cerebral edema. Bleeding occurs due to ruptured blood vessels in the brain due to trauma. Cerebral edema occurs due to the inflammatory phase of brain injury. Lactic acid buildup can also occur due to bleeding, which can lead to impaired cerebral perfusion, resulting in hypoxia, ischemia, and anaerobic cellular respiration. Bleeding in the head area can occur in subdural hematomas, subarachnoid hematomas, intracranial bleeding, and cerebral contusions. Increased intracranial pressure causes clinical symptoms such as decreased consciousness, headache, projectile vomiting, and papilledema. The severity and prognosis of head trauma are also influenced by the location of the trauma. If head trauma occurs at the base of the skull (basal cranial fracture), symptoms that may appear include nosebleeds, ear bleeding, raccoon eyes, and Battle's sign (bruising in the mastoid area). In this condition, the patient requires special attention, monitoring, and intervention (Zia, N. et al. 2019).

Treatment for severe head trauma must be performed quickly and appropriately. Head trauma management includes efforts to prevent excessive increases in intracranial pressure (ICP). ICP management includes head elevation (30°), oxygen administration, and symptomatic medication such as antipyretics, analgesics, and antiemetics. In certain cases where head trauma results in extensive or massive bleeding, immediate evacuation of the bleeding with a craniotomy is necessary. If cerebral edema occurs, the patient should be given osmotic diuretics to reduce intracranial pressure. Brain cells that have been infarcted due to trauma are irreversible, so the only thing that can be done is to reactivate the ischemic area to prevent disability. If head trauma treatment is not carried out appropriately and promptly, the patient's condition will worsen. Factors that cause deterioration in patients with head trauma include age, initial GCS, RTS (Revised Trauma Score), blood pressure, travel time to the hospital, and trauma to other organs. Deterioration in head trauma patients can be seen from the Glasgow Outcome Scale (GOS) (Andrian, A., & Wahyuni, H. P. 2023).

Treatment for patients with head trauma must be initiated immediately. If not treated promptly, the infarct area can expand, causing death or permanent disability. Brain cells that have been infarcted due to trauma are irreversible, so the only thing that can be done is to reactivate the ischemic area to prevent disability. If head trauma is not treated appropriately and promptly, the patient's condition will worsen. Factors that contribute to worsening in patients with head trauma include age, initial GCS, RTS (Revised Trauma Score), blood pressure, and travel time to the hospital (Tito, A. & Saragih, S.G.R. 2018).

Age is the length of time since a person's birth and can be measured using units of time. Normal individuals exhibit similar degrees of anatomical and physiological development. Age influences the healing process in patients with worsening head trauma. Age plays a role in the ability to form new cells and tissues, absorb nutrients, and respond to medications. The younger a person is, the better their healing ability will be; conversely, the older they are, the longer the healing process will take (Coppalini, G., et al. 2023).

GCS is a tool used to measure a person's level of consciousness. It is measured based on three aspects: eye opening, verbal response, and motor response. Head trauma is classified by the GCS score. Mild head trauma has a GCS score of 14-15, moderate head trauma has a GCS score of 9-13, and severe head trauma has a GCS score of less than 8. The GCS assessed is the patient's initial GCS in the hospital's emergency room (Maas, A. I., et al. 2022).

The Revised Trauma Score assesses the overall physiological system of a person. The Revised Trauma Score is administered immediately after a patient is traumatized, typically before hospital admission or during the emergency department. The Revised Trauma Score has been validated as a scoring method for distinguishing patients with a good or poor prognosis. The RTS combines three variables: level of consciousness (GCS), systolic blood pressure (SBP), and respiratory rate (RR). These three variables are categorized into intervals and produce a score ranging from 0 to 12, with higher scores indicating better physiological status. The RTS is categorized as slight (11–12), moderate (8–10), severe (6–7), and serious (1–5). The RTS has been frequently used to predict the prognosis of head trauma, but few studies have linked or combined it with outcome assessment (GOS), thus further research is needed (Padaruntung C. S., et al. 2023).

Blood pressure is the pressure exerted by blood flow in the arteries. The heart beats, typically 60 to 70 times per minute when resting (sitting or lying down), pumping blood throughout the body through the arteries. The highest blood pressure occurs when the heart beats, pumping blood; this is called systolic pressure. Blood pressure reflects the physiological condition and circulatory function of the body. Physiologically, blood pressure is influenced by blood volume and the condition of blood vessels, such as the dilation/constriction phase. Blood pressure also reflects the condition/ability of the heart to contract the heart muscle for the circulation process (Suyasa, I.K., et al. 2019). Head trauma treatment requires immediate medical attention. The principles of first aid are ensuring adequate cerebral perfusion and avoiding increased intracranial pressure. Travel time to the hospital is the time between the trauma incident and first aid being administered at the hospital. This travel time is crucial because the longer the poor cerebral perfusion persists, the worse the patient's prognosis (Golden, N., et al. 2020).

Factors that can worsen the condition of patients with head trauma must be established as early as possible so that appropriate, accurate, and systematic actions and therapies can be immediately implemented to produce a good prognosis/worsening/outcome. The prognosis of head trauma varies from mild trauma to severe permanent neurological deficits and even death. The Glasgow Outcome Scale (GOS) can be used to determine the prognosis of head trauma patients, categorizing them as unfavorable (death, vegetative state, or severe disability) and favorable (moderate GOS score and good recovery). This outcome can be predicted in the first 7 days of treatment as the initial period of head trauma. This prognostic model is expected to assist in allocating resources, making immediate clinical decisions, and providing realistic informed consent regarding the outcome to the patient's family (Jain, S., & Iverson, L. M. 2024). The following are GOS measurements:

Table 1.
The Glasgow Outcome Scale (GOS)

Score	Functional Status	Description
1	Good recovery	Returned to the original functional level and employment with no deficit
2	Moderate disability	Minor neurological defisit that does not interferes with daily functional or work
3	Severe disability	Significant neurological defisit that interferes with daily activities or prevents return to employment
4	Persistent vegetative state	Coma or severe divisit rendering the patient totally dependent
5	Death	Self-explanatory

Preliminary studies/literature studies have shown that head trauma cases are increasing year by year. The annual incidence of head trauma in Indonesia is estimated to reach 500,000 cases. As many as 10% of cases die before arriving at the hospital, 80% are classified as mild head trauma, 10% as moderate trauma, and 10% as severe head trauma. Most head trauma is caused by traffic accidents, especially two-wheeled vehicles (74.6%), followed by four-wheeled vehicle accidents (14.3%) and falls from a height (5.4%). Determining the prognosis of patients with severe head trauma is often difficult, while an accurate prognosis is crucial for providing informed consent. This is due to limitations in initial clinical assessment, the length of recovery in head trauma patients, and the many factors and variables that influence it (Roy, S., at al. 2021).

METHOD

This research is a quantitative study. The research method is comparative analytic with a cross-sectional design. The population in this study were all patients diagnosed with head trauma who were treated at hospitals in the Bali region. The sample is part of the total population. The sample size is related to the precision (accuracy) of the estimation of the influence of the variables studied. The sample size in this study was determined by the Lameshow formula calculation, namely 48 respondents who met the inclusion and exclusion criteria. This study used a sampling technique, namely probability sampling. Respondents were selected using purposive sampling. Data on GOS, age, GCS, RTS, and blood pressure were collected from patient medical records. Data on travel time to hospital were collected from interviews with patients' families. Data analysis was carried out using univariate analysis, bivariate analysis, and multivariate analysis. Bivariate analysis looked at the relationship between factors that cause deterioration in patients with head trauma, and multivariate analysis to find the dominant factor that causes deterioration in patients with head trauma. The multivariate analysis used was the logistic regression test.

RESULT

Data collection was conducted by five enumerators, students currently practicing in hospitals. Data collection took place over three months, from August, September, and October 2024. The following are the results of the data collection in this study:

Table 2.
Description of respondent characteristics

Variable	f	%
Gender		
Male	30	62,5
Female	18	37,5

From table 1 it can be concluded that the incidence of severe head trauma predominantly occurs in male.

Table 2.
Univariate analysis overview

Variable	n	Min	Max	Mean
GOS	48	2	5	3,1 (3)
AGE	48	21 (years)	49 (years)	32,6 (years)
GCS	48	3	7	5,4 (5)
RTC	48	5	7	5,9 (6)
BP	48	70/50 Hg	100/80 mmHg	90/64 mmHg
TIME	48	15 minutes	90 minutes	58,125 minutes

From table 2, it can be concluded that the average GOS score of the study respondents was 3, which means (severe disability). The average age of respondents in this study was 32.6 years. The average GCS score of respondents with severe head injuries was 5. The average RTC score of respondents with severe head injuries in this study was 6 (severe). The average blood pressure of respondents in this study was 90/64 mmHg. The average time required by respondents between the occurrence of head injury and receiving treatment in the emergency room was 58.125 minutes (almost 1 hour).

Table 3.
Bivariate analysis overview

Independent Variables	*p-value*
Age	0,041
GCS (Glasgow Coma Scale)	0,012
RTC (Revised Trauma Score)	0,005
Blood Pressure	0.023
Time to go to the hospital	0,042

From the data above, it can be concluded that the independent variables (age, GCS, RTC, blood pressure, and travel time to the hospital) are related to the dependent variable (GOS). The relationship between the independent and dependent variables can be seen from the p-value, which is ≤ 0.05.

Table 4.
Overview of multivariate analysis

Independent Variables	Coefficient	OR
Age	2,78	1,34
GCS (Glasgow Coma Scale)	1,66	12,46
RTC (Revised Trauma Score)	1,59	16,18
Blood Pressure	2,56	9,64
Time to go to the hospital	1,53	5,45
Constant	1,54	0,04

From the data above, it can be concluded that the independent and dependent variables were subjected to multivariate logistic regression analysis. The multivariate analysis revealed the highest OR value, 16.18 (RTC variable). Therefore, it can be concluded that the most dominant factors influencing the worsening of severe head injury (GOS) are the RTC values (level of consciousness (GCS), systolic blood pressure (SBP), and respiratory rate (RR)).

DISCUSSION

Treatment for severe head trauma must be performed quickly and appropriately. Head trauma management includes efforts to prevent excessive increases in intracranial pressure (ICP). ICP management includes head elevation (30°), oxygen administration, and symptomatic medication such as antipyretics, analgesics, and antiemetics. In certain cases where head trauma results in extensive or massive bleeding, immediate evacuation of the bleeding with a craniotomy is necessary. If cerebral edema occurs, the patient should be given osmotic diuretics to reduce intracranial pressure. Brain cells that have been infarcted due to trauma are irreversible, so the only thing that can be done is to reactivate the ischemic area to prevent disability. If head trauma treatment is not carried out appropriately and promptly, the patient's condition will worsen. Factors that cause deterioration in patients with head trauma include age, initial GCS, RTS (Revised Trauma Score), blood pressure, travel time to the hospital, and trauma to other organs. Deterioration in head trauma patients can be seen from the Glasgow Outcome Scale (GOS) (Mollayeva, T., et al. 2017).

The analysis revealed that the most dominant factors influencing the worsening of severe head injury (GOS) were the RTC scores (level of consciousness (GCS), systolic blood pressure (SBP), and respiratory rate (RR)). The Revised Trauma Score assesses the human physiological system as a whole. The Revised Trauma Score assessment is performed immediately after a patient is traumatized, generally before hospital admission or while in the emergency department. The Revised Trauma Score has been validated as an assessment method to differentiate patients with a good or poor prognosis. The RTS combines three variables: level of consciousness (GCS), systolic blood pressure (SBP), and respiratory rate (RR). The three variables are categorized into intervals and produce a score ranging from 0 to 12, with higher scores indicating better physiological status. The RTS assessment is categorized as slight (11-12), moderate (8-10), severe (6-7), and serious (1-5). The RTS assessment has been frequently used to predict the prognosis of head trauma (Grigorakos, L., et al. 2016).

CONCLUSION

The independent variables (age, GCS, RTC, blood pressure, and travel time to the hospital) have a relationship with the dependent variable (GOS). The relationship between the independent and dependent variables can be seen from the p-value, which is p-value $\leq$ 0.05. The most dominant factor that influences the worsening of severe head injury (GOS) is the value of the RTC (level of consciousness (GCS), systolic blood pressure (SBP), and respiratory rate (RR)) with an OR value of 16.18. Researchers suggest that in assessing the worsening of head injury patients, medical personnel prioritize calculating the RTC value. With the RTC value, health workers can predict the patient's prognosis so that medical treatment can be carried out quickly. For further research, it is hoped that more other factors will be examined and the dominant factors in the worsening of severe head injury patients are found.

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REFERENCES

Adeleye, A. O., & Ogun, M. I. (2017). Clinical epidemiology of head injury from road-traffic trauma in a developing country in the current era. Frontiers in neurology, 8, 695. https://doi.org/10.3389/fneur.2017.00695

Andrian, A., & Wahyuni, H. P. (2023). Perdarahan intrakranial. Jurnal Riset Rumpun Ilmu Kedokteran, 2(1), 150–165. https://doi.org/10.55606/jurrike.v2i1.1064

Coppalini, G., Salvagno, M., Peluso, L., Bogossian, E. G., Quispe Cornejo, A., Labbe, V., ... & Taccone, F. S. (2024). Cardiac injury after traumatic brain injury: clinical consequences and management. Neurocritical care, 40(2), 477-485. https://doi.org/10.1007/s12028-023-01777-3

Golden, N., Mardhika, P. E., Niryana, W., Sukarya, I. M., & Prabawa, I. P. Y. (2020). Risk factors and novel prognostic score for predicting the 14-day mortality of severe traumatic brain injury patients. Intisari Sains Medis, 11(3), 1020-1028. https://doi.org/10.15562/ism.v11i3.831

Grigorakos, L., Alexopoulou, A., Tzortzopoulou, K., Stratouli, S., Chroni, D., Papadaki, E., ... & Sakellaridis, N. (2016). Predictors of outcome in patients with severe traumatic brain injury. J Neurosci Clin Res, 1(1), 1-4.

Husnah, K., Murtala, B., Asriyani, S., Zainuddin, A. A., Mustamir, N., & Latief, N. (2019). Prediksi Prognosis Penderita Trauma Kapitis Berdasarkan Gambaran CT scan Kepala. Jurnal Kedokteran Brawijaya, 30(4), 297-301. http://orcid.org/0000-0002-4790-8089.

Jain, S., & Iverson, L. M. (2024). Glasgow Coma Scale. National Library of Medicine. 13(2), 787. https://doi.org/10.55606/jurrike.v2i1.1064.

Rizkiya, P., Rehatta, N. M., Harijono, B., & Herawati, L. (2020). Analisis Penambahan Dexmedetomidine pada Operasi Besar Tulang Belakang Elektif di RSUD Dr. Soetomo. Jurnal Neuroanestesi Indonesia, 9(2), 78-86. https://doi.org/10.24244/jni.v9i2.225.

Kurowski, B. G., Haarbauer-Krupa, J., & Giza, C. C. (2023). When traumatic brain injuries in children become chronic health conditions. The Journal of head trauma rehabilitation, 38(4), 348-350. https://doi.org/10.1097/htr.0000000000000842.

Maas, A. I., Menon, D. K., Manley, G. T., Abrams, M., Åkerlund, C., Andelic, N., ... & Zemek, R. (2022). Traumatic brain injury: progress and challenges in prevention, clinical care, and research. The Lancet Neurology, 21(11), 1004-1060. https://doi.org/10.1016/S1474-4422(22)00309-X.

Mollayeva, T., Xiong, C., Hanafy, S., Chan, V., Hu, Z. J., Sutton, M., ... & Colantonio, A. (2017). Comorbidity and outcomes in traumatic brain injury: protocol for a systematic review on functional status and risk of death. BMJ open, 7(10), e018626. https://doi.org/10.1136/bmjopen-2017-018626

Padaruntung, C. S., Firdaus, R., Hidayat, A., Kemenkes, P., & Timur, K. (2023). The Correlation Between Revised Trauma Score (RTS) And Head Injury Mortality In The Emergency Room. Formosa Journal Of Science And Technology, 2(7), 1789-1802. https://doi.org/10.55927/fjst.v2i7.5048

Putri, T. I. Y. L., Ahsan, A., Sugiarto, S., Rofiyati, W., Triyono, H. G., Rosyida, R. W., ... & Idrus, F. N. (2021). Perbandingan GAP dan RTS Sebagai Prediktor Perburukan Pasien Cedera Kepala. JI-KES (Jurnal Ilmu Kesehatan), 5(1), 84-90. https://doi.org/10.33006/ji-kes.v5i1.220.

Roy, S., Hawlader, M. D. H., Nabi, M. H., Chakraborty, P. A., Zaman, S., & Alam, M. M. (2021). Patterns of injuries and injury severity among hospitalized road traffic injury (RTI) patients in Bangladesh. Heliyon, 7(3). https://doi.org/10.1016/j.heliyon.2021.e06440.

Suyasa, I. K., Lestari, A. A. W., Prabawa, I. P. Y., & Marta, K. K. A. (2019). Water sport-related spine injury in Bali: a review and preliminary study. Indonesia Journal of Biomedical Science, 13(2). https://doi.org/10.15562/ijbs.v13i2.220

Tito, A., & Saragih, S. G. (2018). Perbandingan glasgow coma scale dan gambaran midline-shift CT-scan kepala sebagai prediktor mortalitas pasien cedera kepala. Cermin Dunia Kedokteran, 45(4), 247-249. https://doi.org/10.55175/cdk.v45i4.796

Zia, N., Mehmood, A., Namaganda, R. H., Ssenyonjo, H., Kobusingye, O., & Hyder, A. A. (2019). Causes and outcomes of traumatic brain injuries in Uganda: analysis from a pilot hospital registry. Trauma surgery & acute care open, 4(1). https://doi.org/10.1136/tsaco-2018-000259.