ORIGINAL ARTICLE

Age, Glasgow Coma Scale and vasopressors as predictors of mortality in traumatized patients treated in the ICU

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Summary

Introduction: Trauma represents one of the most significant problems in public healthcare worldwide. It is one of the leading causes of mortality, particularly among children and young adults, but with a significant majority of non-fatal injuries that result in life-long disabilities and health consequences. Proper and timely identification of patients with a higher risk of mortality is crucial for better outcomes in patients who suffer from trauma. The aim of this study is to identify potential predictors of in-hospital mortality among patients who suffered trauma and are treated in the ICU (Intensive Care Unit).

Methods: The retrospective cohort study was conducted in a trauma, 12-bed ICU at the University Emergency Centre, University Clinical Centre of Serbia, Belgrade. All consecutive patients with blunt trauma were admitted to the ICU between August 2021 and August 2022. The primary outcomes of interest were all-cause in-hospital mortality. A value of $p < 0.05$ was considered statistically significant.

Results: GCS (Hazard ratio 0.924 95%CI 0.873 – 0.979), vasopressors (Hazard ratio 3.47 95%CI 1.373 – 8.787) and age (Hazard ratio 1.030 95%CI 1.014 – 1.047) can independently predict in-hospital mortality.

Conclusion:This study suggests risk factors for unfavorable clinical outcomes after severe

trauma. It may be essential to properly and promptly differentiate between individuals with lower

prognoses, which can lead to prompt and more aggressive treatment of these patients and might

decrease in-hospital mortality. Age, vasopressors and mechanical ventilation, in particular, may be helpful indicators of in-hospital mortality of traumatized patients treated in the ICU.

Keywords: GCS, age, vasopressors, ICU

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INTRODUCTION

Trauma represents one of the most significant problems in healthcare worldwide and, as such, is a great socioeconomic burden. It is one of the leading causes of mortality, particularly among children and young adults, but with a significant majority of non-fatal injuries that result in life-long disabilities and health consequences. Another noteworthy aspect of trauma are its long-term psychological health effects (1).

Several factors are identified as hallmarks of trauma lethality, so it could be predicted if death would occur within minutes, hours, or weeks after trauma. The leading cause of death following trauma is typically severe damage to the central nervous or cardiovascular systems. However, in ICU settings, death is more commonly attributed to sepsis or multiple organ failure (MOF) (2).

Studies have revealed a number of risk factors for the development of MOF, which can lead to death. The most common factors that stand out are age, gender, weight, head injury, traumatic coagulopathy and thrombocytopenia, and hemodynamic status of patients when admitted (3,4).

Considering all this, proper and timely identification of patients with a higher risk of mortality is crucial for better outcomes in patients who suffered from trauma. The aim of this study is to identify potential predictors of in-hospital mortality among patients who suffered from trauma and are treated in the ICU.

PATIENTS AND METHODS

Study design and population

The retrospective cohort study was conducted in a trauma, 12-bed ICU at the Emergency Centre, University Clinical Centre of Serbia, Belgrade. All consecutive patients with blunt trauma were admitted to the ICU between August 2021 and August 2022. The criteria for the inclusion were patients with blunt trauma who were older than 18 years admitted to ICU, a known mechanism of injury. Exclusion criteria were unknown patient identity, patients treated in another health institution for more than 24 hours, and patients who did not live more than 24 hours upon admission. All the necessary data were taken from the Emergency Center's information system (Heliant). The Institutional Review Board approved the study.

Evaluation upon admission

The patients were initially examined and cared for in the emergency room of the Emergency Center according to the trauma protocol. Vital parameters and prescribed therapy were recorded in the hospital's information system. After the diagnosis and the decision on further treatment, the patients were admitted to the ICU. Upon the admission to the ICU, data collected included sociodemographic characteristics of patients, the mechanism of injury, trauma distribution (head, thoracic, abdomen, etc.), the Abbreviated Injury Scale (AIS) score, the Injury Severity Score (ISS), and the patients underlying diseases. Also, factors such as the Glasgow Coma Scale (GSC), the need for blood products, the use of vasopressors, oxygen support, the need for mechanical ventilation (MV), the need for emergency surgery and clinical characteristics (body temperature, systolic and diastolic blood pressure, HR, SpO2) were recorded. According to the ICU treatment protocol, all patients had laboratory analyses (complete blood count, coagulation status, and biochemical analyses) and arterial gas analyses performed upon admission to the ICU. In addition to these values, all important clinical data about the patients were recorded in the electronic database.

Diagnosis and definition

The AIS is the anatomic scale used most widely for rating injury severity (17,18) and it has been used in conjunction with the ISS to identify the effects of multiple injuries on trauma victims (19). AIS and ISS were used to compare injuries. Severe trauma was defined as ISS above 15. The need for vasopressors was defined as mean blood pressure (MAP) lower than 65 mm Hg despite adequate fluid resuscitation. First line of vasopressors was Norepinephrine, infusion started with 0.05-0.1 mcg/kg/min and titrated upwards to achieve desired blood pressure. As other vasopressor support we used Vasopressin administered at a fixed rate of 0.03 units/min up to 0.04-0.06 units/min and Epinephrin with initial dose 0.01-0.1 mcg/kg/min. The need for oxygen support was defined as SpO2 below 89%. GCS below eight and SpO2 below 89% on O2 therapy were indications for mechanical ventilator support [20]. Indication for emergency surgery was provided by the treating emergency surgeons, neurosurgeons, or traumatologists. Coagulopathy refers to a disorder where the blood's ability to clot is impaired, leading to either excessive bleeding (due to inadequate clot formation) or thrombosis (due to excessive clot formation). In trauma patients, coagulopathy is often multifactorial and can result from tissue injury, shock, consumption of clotting factors, and the body's response to trauma. Coagulopathy in trauma patients is associated with poorer outcomes, including increased morbidity and mortality. Resuscitation protocols for post-traumatic coagulopathy focus on early recognition, targeted interventions, and aggressive management to stabilize and optimize the patient's coagulation status. Massive transfusion was defined as the need for more than ten units of packed red blood cells within 24 hours (21).

Outcomes

The primary outcomes of interest were all-cause in-hospital mortality.

Statistical analysis

Data are presented as the median (interquartile range [IQR]) for continuous variables and as the frequency (%) for categorical variables. The Man-Whitney U test was used for the two-group mean comparisons. Categorical data were compared using the Pearson test or Fisher exact test. Patient characteristics such as age, gender, comorbidity, injury characteristics and severity, and clinical characteristics were analyzed in a univariable Cox regression analysis. Parameters that were associated with higher mortality in the univariable analysis (p < 0.20), were entered in a multivariable model, and Cox regression was performed. Odds ratios with 95% confidence intervals were computed. A value of p < 0.05 was considered statistically significant. All analyses were performed using the SPSS (SPSS Inc. Chicago, USA), version 17.0 for Windows.

RESULTS

Of 193 patients admitted to the ICU during the study period, 148 (76.7%) were males, and the mean age of patients was 50.4±18.7. A total of 51 (26.4%) patients died. The sociodemographic characteristics of patients are shown in **Table 1**. One hundred and forty-two patients (73.6%) had polytrauma, whereas 45 (23.3%) had isolated traumatic brain injury (TBI). There is statistically significant difference comparing ISS score of patients who died and those who survived (p=0.044).

Table 1. Sociodemographic characteristics of patients

	Survivor	No Survivor	p-value
Characteristic	n = 142	n = 51	
Age *median (IQR)*	46 (28.25)	65 (28)	**<0.001**
Gender (males) *n (%)*	112 (78.9)	36 (70.6)	0.23
ISS *median (IQR)*	17.5 (16)	22 (19)	**0.044**
Polytrauma *n (%)*	103 (72.5)	39 (73.6)	0.585
Isolated TBI *n (%)*	33 (23.2)	12 (23.5)	0.966

Bold values are statistically significant.
ISS- Injury Severity Score; Isolated TBI- Isolated traumatic brain injury

In **Table 2** we have presented clinical characteristics of patients. In our study we found statistically significant difference compering the patients who survived and those who did not in terms of Glasgow Coma Scale (p<0.001), the need of mechanical ventilation (p<0.001) and vasopressor support (p<0.001).

The laboratory characteristics of our patients are shown in **Table 3**. Statistically significant difference, between the group of survivors and those who died, was only in terms of Oxygen saturation measured in arterial blood gases (p=0.006)

A Cox regression analysis was performed to ascertain the prediction of patients' characteristics on in-hospital mortality. The multivariate Cox regression model was statistically significant, $\chi^2(4) = 57.803$, $p < 0.001$. **Table 2** shows the univariate and multivariate Cox regression of predictors of in-hospital mortality. GCS (Hazard ratio 0.924 95%CI 0.873 – 0.979), vasopressors (Hazard ratio 3.47 95%CI 1.373 – 8.787) and age (Hazard ratio 1.030 95%CI 1.014 – 1.047) independently predict in-hospital mortality.

Table 2. Clinical characteristics of patients

	Survivor	No Survivor	p-value
Characteristic	**n = 142**	**n = 51**	
GCS *median (IQR)*	15 (1)	9 (10)	**<0.001**
SAP *median (IQR)*	130 (34.5)	130 (70)	0.381
DAP *median (IQR)*	80 (21.75)	80 (37)	0.839
MAP *median (IQR)*	97 (25.5)	97 (41)	0.624
HR *median (IQR)*	94 (26)	87 (39)	0.266
P/F ratio *median (IQR)*	395.45 (272.73)	295.45 (292.27)	**0.008**
Vasopressors *n (%)*	26 (18.3)	45 (88.2)	**<0.001**
Mechanical ventilation *n (%)*	56 (39.4)	50 (98)	**<0.001**
Erythrocyte transfusion ≥ 10 unites *n (%)*	8 (5.6)	4 (7.8)	0.575
FFP transfusion ≥ 10 unites *n (%)*	8 (5.6)	5 (9.8)	0.308
Tr transfusion ≥ 10 unites *n (%)*	12 (8.5)	8 (15.7)	0.146
Cryoprecipitate transfusion ≥ 10 unites *n (%)*	28 (19.7)	10 (19.6)	0.968

Bold values are statistically significant.
GCS- Glasgow Coma Scale; SAP- Systolic arterial pressure; DAP- Diastolic arterial pressure; MAP-Mean arterial pressure; HR-Heart rate; P/F- Ratio of arterial oxygen partial pressure to fractional inspired oxygen; FFP transfusion-Fresh frozen plasma transfusion; Tr transfusion - Platelet transfusion

DISCUSSION

Trauma is still one of the leading causes of death for people under the age of 40 in Europe, despite differences in geography, lifestyle, sociopolitical factors, and economic environment, although mortality rates vary widely between countries (5). Other examples of trauma are non-fatal injuries that result in life-long disabilities and health consequences. Therefore, it is very important to identify predictors of lethal outcomes from trauma in the ICU.

In this study, we observed that lethal outcomes happened more often in elderly patients. This finding is supported by other studies, which noted that the age over 65 years is an independent risk factor for increased mortality in trauma, controlled for the same Injury Severity Score (ISS) (6–8). The breakdown of homeostatic mechanisms due to ageing may mask injuries and their severity, making clinical assessment and treatment more difficult. Medications such as beta-blockers, anticoagulants, and steroids can mask the compensatory phase of the shock response. Additionally, conditions like renal and hepatic impairment, chronic steroid use, or a history of malignancy can increase mortality risk in elderly trauma patients by up to fivefold (9).

Table 3. Laboratory characteristics of patients

	Survivor	No Survivor	p-value
Characteristic	**n = 142**	**n = 51**	
Le *median (IQR)*	13.85 (6.25)	15.1 (7.68)	0.48
NLR *median (IQR)*	13.67 (10.11)	14.13 (9.94)	0.309
Hgb *median (IQR)*	119 (27)	122 (24)	0.328
HCT *median (IQR)*	0.36 (0.08)	0.37 (0.07)	0.221
INR *median (IQR)*	1.07 (0.22)	1.11 (0.28)	0.844
aPTT *median (IQR)*	23.1 (4.62)	23 (3.87)	0.566
Fibrinogen *median (IQR)*	2.4 (0.95)	2.55 (1.3)	0.413
Cr *median (IQR)*	80.5 (31)	85.5 (38.25)	0.34
Gly *median (IQR)*	7.2 (3.33)	7.6 (2.93)	0.134
AST *median (IQR)*	65 (71)	66 (86.5)	0.313
ALT *median (IQR)*	47 (53.25)	45 (49)	0.801
pH *median (IQR)*	7.36 (0.11)	7.37 (0.11)	0.748
pCO_2 *median (IQR)*	4.98 (1.19)	4.87 (1.28)	0.941
sO_2 *median (IQR)*	99 (2.15)	98.05 (3.5)	**0.006**
HCO_3 *median (IQR)*	21.4 (5.15)	21.5 (5.2)	0.463
BD *median (IQR)*	-3.7 (5.75)	-3.4 (6.15)	0.809
LAC *median (IQR)*	2.1 (1.98)	2.4 (1.65)	0.291
CRP *median (IQR)*	2.1 (6.65)	2.4 (3.8)	0.585

Bold values are statistically significant.

Le- leukocytes; NLR-Neutrophil to Lymphocyte Ratio; Hgb-Hemoglobin; HCT-Hematocrit;INR- international normalized ratio; aPTT- Activated Partial Thromboplastin Time;Cr- Creatinine; Gly-Glycemia; AST- aspartate aminotransferase; ALT- alanine aminotransferase; pCO2- partial pressure of carbon dioxide ;sO2- Oxygen saturation;HCO3- bicarbonate- Base deficit; LAC-Lactate; CRP- C-reactive protein

There is evidence for gender differences in the morbidity and mortality following trauma. Male gender and advanced age significantly increase the risk of infections and multiple organ failure following trauma and blood loss (10). Bösch et al. suggested the beneficial effects of estrogen for the central nervous system, cardiopulmonary system, liver, kidneys, and overall survival. Also, estrogen enhances humoral and cell-mediated immune responses that could be beneficial in case of major trauma because of the increased activity of macrophages (11).

The severity of trauma is directly correlated to death rates among traumatized patients. The assessment can be made by determining various parameters that are combined into point scales widely used today. One of the most important is the Glasgow Coma Scale (GCS) (12). Among others, GCS was one of the scores that we used in the assessment of our patients. Lower scores on the scale were parameters that were distinguished as a risk factor for late death in trauma patients. Ian Maconochie et al. (13) pointed out an association between the score values and the possible outcome in patients who had suffered a head injury. They found out that death occurs in one-third of patients due to severe injury and lower values of GCS (GCS < 8), while in 20%, it will lead to permanent disability.

Another significant score that is used for evaluating trauma patients is the injury severity score (ISS). As for its role as a predictor of lethal outcomes in trauma, the ISS has demonstrated utility in assessing the overall severity of trauma and has been associated with mortality risk. Higher ISS values generally indicate a more extensive and severe injury burden, which may correlate with an increased risk of mortality. ISS has limitations because multiple injuries within the same body region are only assigned a single score and this may underestimate the severity for the trauma patients. However, it's important to note that the ISS alone may not provide a comprehensive prediction of lethal outcomes, as other factors such as age, pre-existing health conditions, and the timeliness and quality of medical care also play significant roles (14-16).

Tracheal intubation of severely injured patients is mandatory on some occasions, such as severe craniocerebral trauma, multiple rib fractures, and severe shock. A higher ISS score and a lower GCS score are predictors of the duration of mechanical ventilation and the length of hospitalization (17,18). However, mechanical ventilation can bring some complications, such as ventilator-associated pneumonia, which is a known independent risk factor for mortality in the ICU (19). There are several explanations for this, where it is pointed out that traumatized patients suffer persistent inflammation, immunosuppression, and catabolism

Table 4. Univariate and multivariate Cox regression of predictors of in-hospital mortality

	Univariate			Multivariate		
Characteristic	**Hazard ratio**	**CI**	**p - value**	**Hazard ratio**	**CI**	**p- value**
Age	1.032	1.016 – 1.048	**<0.001**	1.030	1.014 – 1.047	**<0.001**
ISS	1.007	0.983 – 1.032	0.572			
sO_2	0.947	0.895 – 1.001	0.056			
GCS	0.916	0.868 – 0.967	**0.002**	0.924	0.873 – 0.979	**0.007**
P/F ratio	0.999	0.997 - 1	0.159			
Vasopressors	8.146	3.45– 19.24	**<0.001**	3.47	1.373 – 8.787	**0.009**
Mechanical ventilation	19.877	2.726– 144.90	**0.003**	5.053	0.597 – 42.787	0.137

Bold values are statistically significant.

ISS- Injury Severity Score; sO2- Oxygen saturation; GCS- Glasgow Coma Scale; P/F ratio- Ratio of arterial oxygen partial pressure to fractional inspired oxygen;

syndrome (PICS). Consequently, they can be more vulnerable to multi-drug-resistant nosocomial infection than other critically ill patients in the ICU, despite equal exposure to invasive devices and to the particular local distribution of microbiota (22). Also, patients with traumatic injuries could experience two types of ARDS. Early-onset ARDS takes place during the first 48 hours after hospital admission due to blood polytransfusion, and late-onset ARDS occurs later, being often associated with multiple organic failures and pneumonia (23). The results of our work support these findings. It has been shown that patients requiring mechanical ventilation have a higher likelihood of poorer outcomes.

Due to massive bleeding, which follows trauma, hemorrhagic shock may occur. The first step in shock resuscitation is to restore mean arterial pressure and systemic blood flow to prevent regional hypoperfusion and tissue hypoxia. Fluid resuscitation is the first strategy applied to restore mean arterial pressure in hemorrhagic shock. However, vasopressor agents may also be needed (24). Although these medications effectively improve hemodynamic parameters, they are also associated with important side effects such as increased myocardial oxygen consumption, myocardial ischemia, and arrhythmias (25). There are numerous studies, as well as ours, that concluded that the use of vasopressors is associated with increased mortality in patients with trauma (26–28). It can be explained in terms of the fact that most severely injured people deny this kind of therapy and that it also has significant side effects that can lead to a lethal outcome.

Acute traumatic coagulopathy is identified in 10 – 34% of traumatizing patients, and it has been associated with increased mortality rates (29). Fibrinogen plays an important role in coagulation by forming stable blood clots. Low fibrinogen levels or inefficient fibrinogen utilization may adversely impact patient outcomes. There are some identified factors that are affecting the level of fibrinogen in major trauma. First of all, lower levels are seen in massive bleeding because of increased utilization. In hypothermia, the synthesis of fibrinogen is affected, and acidemia following hypoperfusion could lead to an increased breakdown of fibrinogen. It is important to say that crystalloid fluids and synthetic colloids can lead to relative hypofibrinogenemia, impacting its function (30, 31). Current European guidelines recommend fibrinogen substitution with cryoprecipitate, fresh frozen plasma, or fibrinogen concentrate at fibrinogen concentrations less than 1.5 to 2.0 g/l during uncontrolled bleeding (24). Surprisingly, our study raises the inconsistent finding that fibrinogen isn't an independent risk factor for lethal outcomes.

Coagulopathy leads to increased transfusion requirements, significantly affecting both morbidity and mortality. Mortality rates rise in the initial hours after trauma patients with uncontrolled hemorrhage due to the "lethal triad"—a combination of coagulopathy, acidosis, and hypothermia—reinforcing each other in a detrimental cycle. The majority of trauma patients develop coagulopathy within two hours. Recognizing coagulopathy early is crucial, prompting the rapid activation of the massive transfusion protocol (MTP) with the hope of preventing death by interrupting the lethal triad before it becomes irreversible. Most deaths associated with MTP occur within the first 6 hours of trauma, with some studies reporting a fourfold increase in mortality when coagulopathy is present. Astonishingly, our results did not designate with these findings. Given that trauma-induced hemorrhage is a leading preventable cause of death worldwide, trauma-induced coagulopathy (TIC) is addressed by promptly administering fresh frozen plasma (FFP), platelets, and other high-dose blood components. Specific massive transfusion protocols are designed to deliver high volumes of blood products in a standardized manner, often using a 1:1:1 ratio of packed red blood cells (PRBC), platelets, and FFP, closely resembling whole blood, especially since whole blood may not be widely available (32). However, no studies to date have addressed the cause of death after MTP (33).

Some limitations of this study should be mentioned. The sample size of this study is relatively small, and being a single-center retrospective study further limits its ability to detect differences between groups. Residual confounding due to unmeasured confounders such as comorbidities and infections. The reason for this is their absence in the health information system. Also, one of the limitations is that at the time we did not do viscoelastic tests for every patient in need of transfusion. We relied on monitor coagulation parameters, clinical response to interventions, and ongoing bleeding. Furthermore, due to the retrospective nature of the study, we did not conduct dynamic assessments of variables. Including this data might reveal more information and strengthen the validity of our research. However, our research was conducted at a Level 1 Trauma Center, the leading academic emergency referral center in our country, serving not only central Serbia but also several neighboring countries.

CONCLUSION

This study added to the increasing body of research that suggests risk factors for unfavorable clinical outcomes after severe trauma. It may be essential to properly and promptly differentiate individuals with lower prognoses, which can lead to prompt and more aggressive treatment of these patients and might cut in-hospital mortality. Age, vasopressors and Glasgow Coma Scale, in particular, may be helpful indicators of in-hospital mortality of traumatized patients treated in the ICU. Additional prospective multicenter research is required on this topic.

Author contributions

Sanja Ratković and Adi Hadžibegović have equal contribution in writing.

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UZRAST, GLAZGOVSKA SKALA KOME I VAZOPRESORI KAO PREDIKTORI SMRTNOG ISHODA KOD PACIJENATA SA TRAUMOM LEČENIH U JEDINICI INTENZIVNOG LEČENJA

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Sažetak

Uvod: Trauma predstavlja jedan od najznačajnijih javnozdravstvenih problema širom sveta. Ona je jedan od vodećih uzroka smrtnosti, posebno u populaciji mladih, ali sa značajno većim udelom nefatalnih povreda koje rezultiraju doživotnim invaliditetom i zdravstvenim posledicama. Pravilna i blagovremena identifikacija pacijenata sa većim rizikom od mortaliteta je ključna za bolje ishode. Cilj ove studije je da ispita potencijalne prediktore smrtnog ishoda kod pacijenata koji su doživeli traumu, a leče se u jedinici intenzivnog lečenja.

Metode: Retrospektivna kohortna studija je sprovedena u traumatološkoj, 12-krevetnoj intenzivnoj intenzivnoj pomoći Univerzitetskog urgentnog centra Kliničkog centra Srbije, Beograd. Svi uzastopni pacijenti sa tupim traumama primljeni su u intenzivnu intenzivnu terapiju između avgusta 2021. i avgusta 2022. Primarni ishodi od interesa bili su bolnička smrtnost od svih uzroka. Vrednost $p < 0{,}05$ smatrana je statistički značajnom.

Rezultati: *GCS* (koeficijent opasnosti 0,924 95%CI 0,873 – 0,979), vazopresori (koeficijent opasnosti 3,47 95%CI 1,373 – 8,787) i starost (koeficijent opasnosti 1,030 95%CI 1,030 95%CI 1,0147 individualno) su se istakli kao najznačajniji nezavisni prediktori smrtnog ishoda.

Zaključak: Ova studija ukazuje na faktore rizika za nepovoljne kliničke ishode nakon teške traume.To može biti od izuzetnog značaja da bi se na vreme izdvojili pojedinci sa lošom prognozom, kako bi se što pre započela adekvatna intenzivna terapija i time smanjila smrtnost. Starost, vazopresori i mehanička ventilacija nezavisno mogu biti prediktori letalnog ishoda kod pacijenata koji su preživeli traumu, a leče se u jedinici intenzivnog lečenja.

Ključne reči: *GCS*, starost, vazopresori, intenzivno lečenje

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