








# Relationship between platelet indices and red cell distribution width and short-term mortality in traumatic brain injury with 30-day mortality

Onur Palabiyik<sup>1\*</sup> , Yakup Tomak<sup>2</sup> , Muberra Acar<sup>3</sup> , Unal Erkorkmaz<sup>4</sup> , Ayca Tas Tuna<sup>1</sup> ,  
Kezban Ozmen Suner<sup>5</sup> , Davut Ceylan<sup>6</sup> 

## SUMMARY

**OBJECTIVE:** This study aimed at investigating whether there is a relationship between 7- or 30-day mortality and mean platelet volume, platelet distribution width, platelet count-to-total lymphocyte count ratio, or red cell distribution width in patients with traumatic brain injury.

**METHODS:** We retrospectively analyzed intensive care unit patients with traumatic brain injury. We recorded patients' ages; genders; diagnoses; Glasgow Coma Scale scores; length of intensive care unit stay (in days); mean platelet volume, platelet distribution width, platelet count-to-total lymphocyte count ratio, and red cell distribution width values upon hospital admission; and health on the 7th and 30th days of their stays.

**RESULTS:** We analyzed data from 110 patients. Of these, 84 (76.4%) were male and 26 (23.6%) were female. On the 7- and 30-day mortality evaluations, compared to the living patients, the deceased patients had a significantly higher median age and a significantly lower median Glasgow Coma Scale. Thus, increased age and lower Glasgow Coma Scale scores were associated with increased 7- and 30-day mortality rates. Mean platelet volume and platelet distribution width values were similar in living and deceased patients. Platelet count-to-total lymphocyte count ratio values were lower in deceased patients, but this difference was not statistically significant. Within 30 days after traumatic brain injury, deceased patients' red cell distribution width values were significantly elevated in deceased patients compared to those of living patients.

**CONCLUSION:** Mean platelet volume, platelet distribution width, and platelet count-to-total lymphocyte count ratio values were not associated with 7- and 30-day mortality, whereas only elevated red cell distribution width was associated with 30-day mortality.

**KEYWORDS:** Mean platelet volume. Mortality. Red cell distribution width. Brain injuries, traumatic.

## INTRODUCTION

Coagulopathy has an essential role as a prognostic factor in traumatic brain injury (TBI). When coagulopathy develops, the risk of a poor outcome increases. Platelet dysfunction can lead to or result from coagulopathy after TBI<sup>1,2</sup>. Mean platelet volume (MPV), platelet distribution width (PDW), and computable platelet count-to-total lymphocyte count ratio (computable PLR) are essential, but they are straightforward parameters in monitoring platelet activation. Platelet indices play an essential role in determining specific diagnostic or therapeutic methods and in following the treatment process.

To the best of our knowledge, there have been no findings on the relationship between short-term mortality and MPV, PDW, PLR, or red cell distribution width (RDW) values in

patients with TBI. The aim of this study was to investigate the relationships between 7- and 30-day mortality and these values in patients with TBI.

## METHODS

### Subjects

This retrospective study was approved by the local Ethics Committee (2018-E.1561). We scanned the charts of all patients who were admitted to the intensive care unit (ICU) between January 2015 and December 2017. Our 20-bed ICU is a department in which patients with a poor general health condition, hemodynamic instability, and multisystem trauma

<sup>1</sup>Sakarya University, Faculty of Medicine, Department of Anesthesiology and Reanimation – Sakarya, Turkey.

<sup>2</sup>Dogus University, Hisar Intercontinental Hospital, Department of Anesthesiology and Reanimation – İstanbul, Turkey.

<sup>3</sup>Istanbul Umraniye Training and Research Hospital, Department of Anesthesiology and Reanimation – İstanbul, Turkey.

<sup>4</sup>Sakarya University, Faculty of Medicine, Department of Biostatistics – Sakarya, Turkey.

<sup>5</sup>Sakarya University Training and Research Hospital, Department of Intensive Care – Sakarya, Turkey.

<sup>6</sup>Sakarya University, Faculty of Medicine, Department of Neurosurgery – Sakarya, Turkey.

\*Corresponding author: [mdpabiyikonur@yahoo.com](mailto:mdpabiyikonur@yahoo.com)

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are hospitalized and receive third-degree treatment. In this study, we included all patients admitted to our ICU during the study period with head trauma who may have had concomitant multisystem trauma. Only children under the age of 18 years were excluded from the study. We obtained patients' ages, genders, diagnoses, numbers of ICU hospitalization days, and their health on the 7th and 30th days of their stays from the patients' ICU follow-up charts and the hospital information management system. Additionally, we obtained MPV, PDW, RDW, and computable PLR values by examining the initial hemograms taken on patients' admission to our hospital emergency service.

### Statistical analysis

Descriptive analyses were performed to provide information on the study population's general characteristics. The Kolmogorov-Smirnov test assessed the normality of the numerical variables' distribution. Accordingly, the Mann-Whitney U test was used to compare the numeric variables between the two groups. The numeric variables were presented as the median [interquartile range]. A multiple logistic regression model was implemented to determine the risk factors independently associated with 7- and 30-day mortality. We considered a p-value of <0.05 statistically significant. We performed analysis using the SPSS Statistics software (IBM SPSS Statistics, version 23.0., IBM Corp., Armonk, NY, USA).

## RESULTS

During the study period, 137 patients with TBI were hospitalized in the ICU. We excluded 27 patients from the study because they were younger than 18 years of age, and we performed the data analysis on 110 patients.

The participants' mean age was 47.81 ( $\pm 21.5$ ) years. In total, 84 (76.4%) patients were male, and 26 (23.6%) were female. The mean ICU stay length was 29.88 $\pm$ 42.3 days. The mean Glasgow Coma Scale (GCS) score was 6.16 $\pm$ 3.5. Severe TBI had occurred among 75.5% (n=83) of the patients. Of the patients, 45.5% (n=50) had subarachnoid hemorrhage (SAH) alone, 20.9% (n=23) had SAH and epidural hemorrhage (EDH), 14.5% (n=16) had subdural hemorrhage (SDH), 7.3% (n=8) had EDH, 7.3% (n=8) had intracerebral hemorrhage, and 4.5% (n=5) had SAH and SDH. The patients' 7- and 30-day mortality rates were 20.9 and 44.5%, respectively. The descriptive statistics for all variables for patients are shown in Table 1.

There was a significant difference between the patients who died by the 7th day and those who survived until the 7th day in terms of age and GCS. The median age was significantly

higher in the deceased patients than that of the living patients (p=0.003). The median GCS was significantly lower in deceased patients (p<0.001). There was no significant difference between the patients who died by the 7th day and those who survived until the 7th day in terms of the other variables. Although deceased patients had higher RDW and PDW and lower MPV and PLR than living patients, these differences in values were not statistically significant (p>0.05; Table 2).

There was a significant difference between the patients who died by the 30th day and those who survived until the 30th day in terms of age, GCS, and RDW. The median age and RDW level were significantly higher in deceased patients than those in living patients (p<0.001 and p=0.007, respectively). GCS in deceased patients was significantly lower than in living patients (p<0.001). We found no significant difference between the patients who died by the 30th day and those who survived until

**Table 1.** Descriptive statistics for all variables.

Variables	Mean $\pm$ Std	Min-Max
Age (years)	47.81 $\pm$ 21.5	18-91
GCS	6.16 $\pm$ 3.5	3-15
RDW (%)	15.14 $\pm$ 1.5	12.1-20.7
MPV (fL)	7.69 $\pm$ 1.4	5.6-12.8
PDW (%)	18.07 $\pm$ 1.4	16.1-23.8
PLR	101.44 $\pm$ 86.7	21.3-511.0
ICU stay (days)	29.88 $\pm$ 42.3	1-180
Gender	Male	84 (76.4%)
	Female	26 (23.6%)
Diagnosis	SAH	50 (45.5%)
	SAH+SDH	5 (4.5%)
	ICH	8 (7.3%)
	SDH	16 (14.5%)
	EDH	8 (7.3%)
	SAH+EDH	23 (20.9%)
Degree of TBI	Mild/moderate	27 (24.5%)
	Severe	83 (75.5%)
Day 7	Alive	87 (79.1%)
	Deceased	23 (20.9%)
Day 30	Alive	61 (55.5%)
	Deceased	49 (44.5%)

EDH: epidural hemorrhage; GCS: Glasgow Coma Scale; ICH: intracerebral hemorrhage; ICU: intensive care unit; MPV: mean platelet volume; PDW: platelet distribution width; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; TBI: traumatic brain injury; SAH: subarachnoid hemorrhage; SDH: subdural hemorrhage; Std: standard deviation; Min: minimum; Max: maximum. Data were shown as number, count, and percentage.

the 30th day in terms of MPV, PDW, or PLR values ( $p>0.05$ ). PLR values were lower in deceased patients, but this difference was not statistically significant ( $p=0.147$ ; Table 2).

According to the logistic regression models for 7- and 30-day mortality, with a decrease of 1 point in GCS, the probability of death increased by 1.731 times and 1.615 times, respectively (Table 3). On the 7th day, the risk of mortality was 7.253 times higher in men than in women, and mortality in non-EDH diagnoses was 5.435 times higher than that in EDH diagnoses (Table 3).

## DISCUSSION

This study found no relationship between MPV or PDW and 7-day or 30-day mortality. However, RDW was significantly higher in deceased patients within 30 days after TBI. The PLR was lower in deceased patients at both 7 and 30 days, but this

difference was not statistically significant. Increased age and lower GCS scores were associated with both 7- and 30-day mortality.

Traumatic brain injury is an important, life-threatening public health problem and a significant cause of morbidity and mortality in ICU patients. In one study of patients with severe TBI, the 7-day mortality rate was 10%, and the 28-day mortality was 29%<sup>3</sup>. In a study of patients with TBI aged 65 years and older, the 14-day mortality rate was 11.2%<sup>4</sup>. Studies on adults without any age limit have shown that the 30-day mortality rates ranged from 15.3 to 31.5%<sup>5,6</sup>. In young adults between the ages of 18 and 30 years, the 30-day mortality rate has been reported to be 12%<sup>7</sup>. In this study, 7- and 30-day mortality rates were 20.9 and 44.5%, respectively, which are higher than the rates demonstrated in other studies. Both the mean PDW and the mean RDW values of all our living and deceased patients were higher than the standard values, reported as

**Table 2.** Comparison results of the characteristics and other features between two groups for 7- and 30-day mortality.

	Day 7 - alive (n=87)	Day 7 - deceased (n=23)	p	Day 30 - alive (n=61)	Day 30 - deceased (n=49)	p
Age (years)	40 [30]	64 [37]	<b>0.003</b>	38 [27.5]	63 [37]	<b>&lt;0.001</b>
GCS	6 [7]	3 [1]	<b>&lt;0.001</b>	8 [6]	3 [1.5]	<b>&lt;0.001</b>
MPV (fL)	7.5 [1.9]	7.1 [1.6]	0.402	7.5 [1.8]	7.5 [1.6]	0.445
PDW (%)	17.7 [1.7]	18.1 [2.1]	0.298	17.7 [2.05]	17.8 [1.75]	0.500
PLR	83.6 [70.2]	66.2 [25.5]	0.164	85.6 [75.85]	66.8 [52.35]	0.147
RDW (%)	14.8 [1.7]	15.2 [1.9]	0.191	14.6 [1.45]	15.3 [1.8]	<b>0.007</b>
Gender (M/F)	63/24	21/2	0.095	46/15	38/11	0.971

GCS: Glasgow Coma Scale; MPV: mean platelet volume; PDW: platelet distribution width; PLR: platelet-to-lymphocyte ratio; RDW: red cell distribution width; M: male; F: female. Data were presented as median [interquartile range] for continuous variables and as number (percentage) for categorical variables. Bold indicates statistically significant p-value.

**Table 3.** Logistic regression model for 7- and 30-day mortality.

		$\beta$	SE ( $\beta$ )	p	OR	95%CI for OR
Day 7	Age	0.038	0.014	<b>0.008</b>	1.038	(1.01-1.067)
	Gender (male)	1.981	0.877	<b>0.024</b>	7.253	(1.305-41.066)
	GCS	-0.548	0.186	<b>0.003</b>	1.731	(1.202-2.492)
	EDH	-1.692	0.847	<b>0.046</b>	5.435	(1.032-28.571)
	Constant	-2.011	1.350	0.137	0.134	
Day 30	Age	0.042	0.013	<b>0.001</b>	1.043	(1.017-1.069)
	GCS	-0.479	0.110	<b>&lt;0.001</b>	1.615	(1.302-2.003)
	SDH	0.678	0.628	0.280	1.971	(0.576-6.745)
	Constant	0.271	0.774	0.727	1.311	

GCS: Glasgow Coma Scale; EDH: epidural hemorrhage; SDH: subdural hemorrhage;  $\beta$ : regression coefficient; SE: standard error; OR: odds ratio; CI: confidence interval. Bold indicates statistically significant p-value.

increased mortality risk<sup>4,8,9</sup>, and thus supporting our high mortality rate. We thought that the higher mortality rates in our study compared to those in the literature were due to the hospitalization planning of our hospital's TBI patients, our patient population's general health status, the distribution of intracranial hemorrhage diagnoses, and the presence of concurrent multisystem trauma. First, the patients with head trauma admitted to our hospital who had hemodynamic stability and high GCS scores were hospitalized in the surgical ICU, whereas the patients with poor general health, an unstable hemodynamic status, and low GCS scores were hospitalized in our ICU. Concurrent types of intracranial hemorrhage and the comorbidities are associated with high mortality<sup>10</sup>. Moreover, mortality is higher than normal in patients with SAH and SDH<sup>11,12</sup>. In our study, SAH and SDH constituted the majority (~65%) of diagnoses. The mortality increased by approximately 5.4 times in patients diagnosed with intracranial hemorrhages other than EDH. It should also be noted that our study included not only patients with isolated head trauma but also patients with head trauma and concomitant thoracic or abdominal trauma or bone fractures.

Most studies have shown that mortality increases with advancing age<sup>13-15</sup>. In this study, the ages of the patients who died within 7 and 30 days after TBI were significantly higher than those of the patients who survived. Furthermore, according to the logistic regression analysis, age was an independent risk factor for both 7- and 30-day mortality.

Head trauma is mostly seen in men<sup>3,6,13</sup>. Although gender has not been related to mortality<sup>4,14</sup>, several studies have found that females have a higher mortality rate<sup>15,16</sup>. In this study, the number of males was higher than that of female patients. Although the mortality rate was similar in both men and women, the probability of death in men was approximately 6.7 times higher than that in women within the first 7 days after TBI.

Low GCS scores have been associated with an increased risk of death within 7 and 30 days following TBI<sup>13-15,17</sup>. In this study, the mortality rate was higher in patients with a GCS scores of 8 or lower than in patients with higher GCS scores, and a low GCS score was an independent risk factor for both 7- and 30-day mortality.

Platelets are known to be important blood cells in the coagulation system. Coagulopathy development following trauma causes changes in platelet indices<sup>1,8</sup>. Decreased platelet count and platelet dysfunction occur in the pathophysiological process of coagulopathy after TBI and have been associated with increased mortality<sup>1,2,18</sup>. Platelet indices are a group of platelet

biomarkers that serve as easily measurable parameters. MPV, which is an indicator of the average platelet size, increases during platelet activation<sup>19</sup>. Changes in MPV values have been related to a variety of prothrombotic and pro-inflammatory diseases as prognostic factors<sup>19</sup>. An MPV value of greater than 11.3 fL has been reported to be an independent risk factor for mortality in ICU patients<sup>8,9</sup>. MPV values are significantly lower in patients with TBI than in healthy individuals<sup>20,21</sup>. In this study, the MPV values were statistically similar for both deceased and living patients.

Another platelet marker related to platelet activation is PDW. A PDW value between 9 and 14 fL is considered normal, and increased PDW indicates platelet anisocytosis<sup>22</sup>. A PDW value above 17% was an independent risk factor for mortality in ICU patients<sup>8,9</sup>. Zhang et al.<sup>17</sup> reported that PDW levels were higher in deceased patients with TBI than in survivors; nevertheless, Bobeff et al.<sup>4</sup> found that PDW levels were similar in both groups. In this study, the mean PDW value of all patients was above 18%, which was higher than the normal range. The deceased patients had higher PDW values than the living patients, but this difference was not statistically significant.

The PLR was higher among deceased patients than among survivors<sup>23,24</sup>. A higher PLR on ICU admission was associated with a poor neurological outcome at discharge in patients with non-traumatic intracerebral hemorrhage<sup>25</sup>. However, in TBI, a decreased platelet count is commonly seen and is associated with an increased risk of mortality<sup>4,8</sup>. Therefore, it is expected that the PLR will decrease after TBI. Among the ICU patients with TBI included in our study, PLR was lower in deceased patients than in living patients, but this difference was not statistically significant.

Red cell distribution width is an indicator of red blood cells' volume and size changes, and elevated RDW levels are associated with increased mortality<sup>9</sup> and poor neurological outcomes after aneurysmal SAH<sup>26</sup>. In one study, patients with traumatic SAH who died had higher RDW than those who survived<sup>27</sup>, and mortality rates and unfavorable neurological outcomes after SAH have been found to be significantly more common in patients with high RDW on admission<sup>28</sup>. A study that included patients with TBI over 65 years old reported significantly increased 30-day mortality in patients with initial RDW values of 14.5 and above<sup>4</sup>. In this study, the mean RDW value of all patients was above 15%, and, consistent with the literature, RDW was higher in deceased patients than in living patients. Additionally, an increased RDW was associated with increased 30-day mortality.

This study has some limitations. The most important limitation is that it is a retrospective study. The limited number

of included patients due to the study being conducted within a single center represents another limitation.

## CONCLUSION

Intensive care unit patients with TBI have high mortality rates. Age and low GCS scores are independent risk factors associated with increased 7- and 30-day mortality rates. Elevated RDW is associated with 30-day mortality. Contrary to what is reported in other diseases, our patients with TBI who later died demonstrated lower PLR than those who survived. However, this result of the study was not statistically significant. The

results of this study can guide the literature and broaden our horizons for future research.

## AUTHORS' CONTRIBUTIONS

**OP:** Conceptualization, Data curation, Methodology, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. **YT:** Conceptualization, Methodology, Supervision, Writing – review & editing. **MA:** Data curation, Resources. **UE:** Formal Analysis, Validation. **ATT:** Data curation, Resources. **KOS:** Data curation, Resources. **DC:** Data curation, Resources.

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