Can the mean platelet volume predict the mortality of patients with head trauma?

Bulent OZDEMIR[1], Ayhan KANAT[1]*, Hizir KAZDAL[2], Osman Ersegun BATCIK[1], Vacide OZDEMIR[3], Yusuf Sulun[4], Ali Riza Guvercin[5]

[1]--Recep Tayyip Erdogan University, Medical Faculty, Department of Neurosurgery, Rize-Turkey

[2] Recep Tayyip Erdogan University Medical Faculty Department of Anesthesiology and Reanimation Rize-Turkey

[3]- Recep Tayyip Erdoğan University, School of Health, Department of Medical Nursing, Rize, Turkey

[4]-Muğla Sıtkı Koçman University, Educational Faculty, Department of Physical Science, Mugla Turkey

[5]- Karadeniz Technical University, School of Medicine, Department of Neurosurgery, Trabzon, Turkey

***Correspondence:** Ayhan Kanat, MD

Affiliation: Recep Tayyip Erdogan University, Medical Faculty, Department of Neurosurgery, Rize-Turkey

Mail: ayhankanat@yahoo.com Phone: 90 506 5855139

Fax +90 464 2130364

ORCIDs:

1. Author Bulent Ozdemir (Orcid:0000-0002-7635-9808),

2. Author Ayhan Kanat[1,*], (orcid:0000-0002-8189-2877)

3. Author; Hizir Kazdal, (Orcid: 0000-0002-0759-4716)

4. Author Osman Ersagun Batcik (Orcid:0000-0002-6095-3642),

5. Vacide Ozdemir, (Orcid:0000-0001-6421-1518),

6. Yusuf Sulun Orcid 0000-0003-3023-6877

7. Ali Riza Guvercin: Orcid 0000-0002-8689-0571

Abstract

Objective: Prediction of mortality in the patient of the intensive care unit is essential. It was aimed to study the mortality predictive value of mean platelet volume (MPV) in patients with severe head trauma.

Study design: The mean platelet volumes were measured in patients with head injury managed intensive care unit between 1 December 2017 and 1 January 2019 at admission and exitus date.

Methods: The main outcome variable was mortality due to the traumatic event of patients. 43 patients with head trauma admitted to the intensive care unit during the study period. 17 patients died (Group I), 26 survived (Group II).

Results: There was not an association between MPV and mortality at admission. However, Cox regression analysis showed that late MPV (at exitus or discharged date), WBC at admission, and age increase the mortality rate 1,770, 1,202, 1,052 times, respectively.

C**onclusion:** The present study shows that MPV may be a useful predictor of mortality in the patient with severe head trauma. More detailed studies are needed.

Key-words: mean platelet volume; mortality; intensive care unit; head injury

What is already known on this subject;

In critically ill patients, several screening tools of blood parameters have been used to predict the mortality risk of patients, but the timely identification of patients with clinical deterioration may not always possible in a ICU patient with head trauma, accurate prognostication will be valuable. To date, there is not an ideal biomarker for identifying mortality head trauma.

What this study adds;

The present study shows that MPV may be a useful predictor of mortality in the patient with severe head trauma.

Message for the clinic

MPV may be red flags in the management of traumatic patients of the intensive care unit.

Introduction

Background/rationale: Severe traumatic brain injury (TBI) refers to severe injuries of the central nervous system such as skull fracture, brain contusion and laceration and intracranial haematoma[1]. Its prevalence is not low. The burden of TBI is still associated with large medical and socio-economic problems[2], because 2% of the patient with traumatic brain injury live with a traumatic brain injury–related disability[3]. Major changes in the medical practice have been observed in the last decades,[4] [5],[6]. In the 1990s, the advancements in modern diagnostic methods, and medical technologies[7]. Advances in technology have intensely altered the management of patients with head trauma[8]. Despite these recent developments in technology and facilities in the medical practice[9], trauma remains a major public health problem with high morbidity and mortality. Primary or secondary brain injury may occur[10]. The mainstay of treatment in these patients is to prevent secondary brain injuries. In critically ill patients, several screening tools of blood parameters have been used to predict the mortality risk of patients. Serial bedside neurological

examinations in ICU are still an important issue[11],[12], but the timely identification of patients with clinical deterioration may not always possible in a ICU patient with head trauma, accurate prognostication will be valuable. To date, there is not an ideal biomarker for identifying mortality head trauma. Bleeding and hematoma expansion are feared complications in patients of intensive care units. The volume of hematoma is a risk factor in the intracranial pathologies[13], but understanding the underlying mechanisms of these hemorrhage-related complications has potential practical implications by informing clinicians in ICU. Mean platelet volume (MPV shows the mean size of thrombocytes and thrombocyte activation[1]. The impaired clot formation may be associated with mortality and morbidity in trauma patients, suggesting the increased mean platelet volume (MPV) may be a marker in predicting the mortality and morbidity after head trauma in ICU patients. It is a well-known platelet parameter, its measurement is based on the size of the platelets in the peripheral blood, can be assessed in routine blood samples[1], because it platelet count is part of the complete blood count. It is inexpensive and readily available in emergency rooms. The catecholamine surge in after general trauma may contribute to abnormal mean platelet volume,and may indicate the overall mortality in the intensive care unit, because higher mean platelet volumes indicate increasing on platelet activity and hypercoagulopathy. Intensivists should be familiar with the complications in ICU, may determine the neurological status of critically ill patients through the use of neurological examination[14]. For that reason, several scoring systems have been used for the evaluation of disease severity and mortality rates of patients wih brain injury and in ICU, such as the simplified acute physiology score II (SAPS II), the acute physiology and chronic health evaluation II (APACHE II), the OMEGA score system. The APACHE II model has been often used in the risk stratification of patients of ICU. However, this model uses the lowest values of 12 measured physiological variables during the first 24 h after admission in the ICU, with the evaluation of the patient's chronic

health and the diagnosis at admission, to predict mortality. So it is valuable during the first 24 h after admission. This is a disadvantage of the model. Any contribution to our knowledge of the cause of mortality of patients with severe head trauma in intensive care units is always welcome. This subject was investigated.

Subjects and Methods

This study was approved by the local Ethical Committee (Decision No:2017/173; 23.11.2017)

Study design and setting

All patients are managed in the intensive care unit between 1 December 2017 and 1 January 2019. Patients were divided into two groups as the nonsurvived or died patients group I, survived group II. Inclusion criteria were a valid MPV, adult age >18 years, and, admitted after severe head trauma. The nontraumatic patient was not included. Also, patients with hematocrit less than 0.30 or greater than 0.52, a platelet count under 100.000, and over 450.000/mL at admission were excluded from the study. The patients had no clinical evidence of other systemic diseases, infection and were not taking medications known to affect platelet function.

MPV Determination

Blood samples were routinely taken every day in our intensive care unit. MPV and WBC measurements at admission and the day of mortality were evaluated. EDTA blood samples were drawn from each subject by antecubital venipuncture. These blood samples were analyzed in an automated hematology analysis system (Abbot Diagnostic Ruby Cell-Dyn 5440 Patrick Henry Dr. Santa Clara CA 95054, USA).

Determination of Outcome Variable and Statistical Analysis

Statistical evaluation was performed by the statistical package for the social sciences (SPSS) version 20 (Chicago, IL) for Windows statistics program. Data were expressed as

mean ± standard deviation. The main outcome variable was mortality and discharging APACHE II scores of the patient from ICU. The APACHE II score that has been the gold standard in ICU which demonstrates the mortality risk of the ICU patients. Correlation of APACHE-II, GCS scores the MPV levels at the admission and discharge were performed.

Results

Participants: 43 patients with head trauma were included in the study. Of those, 17 patients died (Group I). 26 patients were survived (Group II), MPV values compared. 83,1% (36 patients) were male and 16,9% (6 patients) were female. Figure 1 shows the survival analysis of patients

Descriptive data: The mean age of group I and II were 58,59 and 41,08 with statistical significance p=0,03<0.05. The median age at the time of death was 58,5 years. The average days of exitus was 9,7 days. The average exitus date and day of discharging from the critical care unit and of group I and II patients were 11,69 and 9,71: respectively. Days in ICU, MPV values at admission and exitus date, WBC at admission and discharged or exitus date of patients were shown in table 1, there is no statistically significant difference between male and female patients, but the mortality rate is higher in males patients (n=12) than female patients (n=5). Duration in the intensive care unit was not statistically significant between groups (P=0,575>0.05). Descriptive statistics included mean, SD, median, minimum, and maximum for all continuous variables as these variables were non-normally and normally distributed. Shapiro–Wilk test was used to test for the normality distribution of continuous variables. For continuous variables, we used the Repeated ANOVA Test for comparing two groups. We used the chi-square test for categorical variables. A p-value<0.05 was considered statistically significant. Survival analysis was examined. If the patient is still alive, overall survival is taken the day of discharging the patient from the ICU unit. If a patient has died, the end date is the date of death. Mortality was accepted as the reference value. The dependent

factors on mortality and survival status were tested by binomial logistic regression analysis. Mortality was accepted as the reference value. Binomial logistic regression analysis showed that late MPV (at exitus or discharged date), WBC at admission, and age increase the mortality rate 1,770, 1,202, 1,052 times, respectively (Table 2). The receiver-operating characteristic (ROC) curve and the area under the ROC curve (AUC) were used to discriminate discharged cases from dead patients. Based on Youden's index, the best cut off value for each parameter was determined. We calculated the best cut off value based on Youden's index and the sensitivity and specificity in those criteria. In the ROC analysis, the precision of MPV measurements in predicting mortality was moderate and the area under the curve(AUC) was 0.76 (95% CI: 0.61- 0.88) with a sensitivity and specificity of 94,12% (95% CI: 71,3- 99,9) and 57,6% (95% CI: 36,9- 76,6).For WBC the area under the curve(AUC) was 0.70 (95% CI: 0.54- 0.83) with a sensitivity and specificity of 47,06% (95% CI: 23,0- 72,2) and 92,31% (95% CI: 74,9- 92,1) Table 3,4 and Figure 2. In both values, the best cutoff values for mortality were 7,1 and 16,8, and statistically, a significant difference was observed($p<0,05$),

Discussion

Key results: In the present study, we investigated the impact on the mortality of MPV of patients managed in the intensive care unit after head trauma. Increased MPV may be risk factors for patients with head trauma.

Our clinical practice is being guided by scientific principles[15][16]. The human cranium anatomy with clivus is important[17]. The thick clivus protects the structure of human cranium. Despite the anvantage of cranial anatomy, trauma with high morbidity and mortality is still an important public health problem. Mortality assessment after head trauma is important to predict the outcome of patients in ICU. Our study has one important finding. Despite having similar MPV values on admission, non-survivors had higher MPV than did

survivors after admission Cox regression analysis showed that late MPV (at exitus or discharged date), WBC at admission, and age increase the mortality rate 1,770, 1,202, 1,052 times, consecutively (Table 2).

The head injury has the greatest impact on the mortality of trauma patients in ICU. Efforts were focused on detection, reduction, and prevention of causes of mortality and morbidity. ICU patients require close monitoring[14]. Quantitative and clinically relevant surrogate outcome measures are needed in ICU. In this context, severity scales such as The APACHE II are important adjuncts of treatment in the ICU. However, the APACHE score emphasizes the measurement of physiological derangement, and there is a small consideration of preexisting disease and may not adequately account for the quantitative or qualitative contribution of comorbid illness (e.g., the APACHE II system assigns 0, 2, or 5 chronic health points for preexisting comorbidity out of a possible 73 total points), thus limiting the ability of these model to accurately predict mortality. For that reason, another predictor of clinical outcome should be determined. In this study, we found that there was no correlation between trauma pattern as well as systemic injury and MPV at admission. MPV can be affected by many parameters. We studied the number of parameters such as blood transfusions, hemoglobin, and hematocrit levels, blood pressure, temperature, pulse rate. There was no difference in these parameters between survived and nonsurvived patient groups. Also, platelets can be affected by inflammation, however, in this study, WBC counts were different between study groups only at the admission (Table 1).

Survival analysis is important. We used the overall survival as the length of time from the admission of ICU after head trauma to the discharging time of the patient. If the patient is still alive, overall survival is taken the day of discharging the patient from the ICU unit. If a patient has died, the end date is the date of death. The result of the binomial logistic regression analysis and survival graphic were given in table 2 and figure 1. In this study,

statistically different early WBC at admission may be explained by the effects of the adrenergic system after traumatic events. Higher MPV may be observed in systemic diseases. Primary thrombocythemia is a chronic proliferative disorder of the bone marrow in which either thrombotic or paradoxically hemorrhagic symptoms or both may occur due to the pathological increase in the number of platelets. Only one case with primary thrombocythemia and chronic subdural hygroma was reported in the literature[18]. This mentioned pathologies above may increase the risk of mortality in intensive care units after trauma, for that reason the patients with these pathologies were excluded from this study. There were no infections, disseminated intravascular coagulation, etc, which may influence MPV levels.

Interpretation

Importance of the Present Study

In medical literature, there is no study about mean platelet volume as a mortality predictor in traumatic patients of the intensive care unit. Our study is the first report which shows that there are no differences of MPV at the admission between two groups, but there is a statistically significant difference between the level of the exitus or the discharged date. The recognition of this fact is important. If indeed one is the first to report something and that something is of value [19]. Males' and females' brains develop differently[20]. There was no gender difference of the day in ICU, MPV values at admission and exitus date, WBC between at the admission values and discharged or exitus date values, but in this study, the mortality rate is higher in males patients (n=12) than female patients (n=5). In died patients (group I), the means day of intensive care management was 8,3 days in males, 13 days in females, but the difference is not statistically significant.

Generalisability

Our study showed that MPV may be a practical and prognostically predictor of mortality of patients in the intensive care unit at the exitus date, but we could not detect this difference at the admission date. The present study also contributes to some concern(s) about cardiovascular drugs, such as beta-blockers. These drugs may influence platelet function, and these additional effects may influence the treatment outcome of trauma patients in critical care units. The effects of various drugs on platelet size in ICUs are an important issue such as clopidogrel.

To examine the outcomes of therapy, it is necessary to have testable hypotheses. Outcomes are then expressed concerning the implied goals[21], but there is no human study that shows an association of increased MPV and mortality in patients with head trauma. By preventing the activation of platelets, carotid thrombosis and intimal hyperplasia can be impeded[22]. Our study suggests that platelet-related drugs such as aspirin and clopidogrel should be used in intensive care units with caution. Hypothermia has been used in the intensive care unit to control the rise in ICP associated with head trauma. Hypothermia may affect the MPV values of patients. This subject should be investigated. MPV may be red flags in the management of traumatic patients of the intensive care unit. In some contexts, red flags mean that something important that needs to be brought to the immediate attention[23].

Strengths and Limitations of the Present Study

This study is a single-center retrospective, observational study with relatively small sample size. One of the limitations is the low sample size and the retrospective nature of the study. We think the series is not large enough to justify our result. The sample size of a study is an important issue[24]. If a researcher selects fewer samples it may lead to missing any significant difference even if it exists in the population[25]. These results must, therefore, be validated by further studies utilizing much larger population samples to determine its wider significance. In the present study, the increases in MPV in the trauma patient in the critical

care unit cannot be fully explained by haemoconcentration, because the average duration in the intensive care unit is 9,71 and 11,69 days for the group I and II, respectively. Duration in intensive care unit patients was not statistically different between the two groups of the study. The non-survivors were older, with a higher APACHE score and lower GCS than the survivor group; increased age and severity of illness are predictable factors associated with increased mortality. No direct comparison with other prognosis factors has been performed. For example, elevated intracranial pressure is one of the important causes of mortality in patients with severe traumatic brain injury. We did not obtain the ICP values of patients. This may be an important limitation of our study, but we daily examined the papilledema. The cases with papilledema (likely with increased ICP) were excluded from the study. In this study, we did not use the GCS scores. The Glasgow Coma Scale was originally devised for research on patients with impaired consciousness or coma mainly caused by head trauma[26]. It has become the worldwide standard in the assessment of the patient in ICU. Sedation is frequently used in patients of ICU. The GCS has repeatedly been criticized for its several failures to reflect verbal reaction in intubated patients[14] as in patients of ICUs. Other limitations are; the retrospective study design is prone to bias, and we are unable to adjust for risk factors such as plasma catecholamine levels and other markers of platelet activation which were not measured. Plasma catecholamine levels and other markers of platelet activation may be increased following trauma. In the late phase of trauma, the association of MPV with mortality of patients is an important causal relationship. Another limitation, a broad spectrum of MPV values was seen in our analysis, ranging from 6.5 fL to 11.75 fL groups I and II, respectively. Several factors like as partially clotting of the specimen with activation and aggregation of platelets during venipuncture may affect the correct measurement MPV. Besides, it should not be forgotten that increased MPV levels were observed in several

diseases such as cerebrovascular disease, peripheral artery disease, malignancy, inflammatory diseases.

Given the significant but still narrow absolute difference in mean values of MPV between dead and survived patients, the clinical utility of an isolated MPV value in determining an individual's mortality risk should be investigated in larger studies. The intracranial hematoma volume is also an important issue[27]. It is difficult to assess the relationship between the days when the MPV is rising with the outcome of this study because seven of 17 patients (group1) died in two days. Another important limitation is the lack of difference in MPV on admission. For the prediction of mortality, early markers at admission are needed.

Conclusions

A comprehensive understanding of the pathophysiology is paramount in medical practice[28]. We aimed to investigate the relationship between mean platelet volume (MPV) and the mortality of patients with severe head trauma and found that nonsurvivors had a greater mean platelet volume during their stay in the ICU compared with that of survivors on discharge. The cause of this greater lifespan and their impact on mortality is an important finding of the present study. It can be lead to relevant interrogations for example regarding the balance between thrombosis and fibrinolysis in trauma patients of ICU patients, so it concluded that MPV may be a useful predictor biomarker in the patient with severe head trauma. We suggest that the increased MPV has a predictor role for mortality in traumatic patients of critical care units only after several days of trauma. Whether the relationship is causal, or not, remains unknown. However, our finding is important. More studies are needed.

Abbreviations

CCU: critical care unit

GCS: Glasgow coma scale

ICP: Intracranial pressure

MPV: Mean platelet volume

TBI: Traumatic brain injury.

Conflict of Interest: None

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Legends

Figures

Figure 1 shows the survival analysis of patients

Figure 2 Area under the receiver operating characteristic curves (AROC) for discriminating between died and discharged patients

Tables

Table 1 shows the days in ICU, MPV values at admission and exitus date, WBC at admission and discharged or exitus date, and gender of patients. Early MPV and WBC mean the MPV and WBC at the admission date, late MPV and WBC are the MPV and WBC at discharged or exitus date.

Table 2: Binomial logistic regression analysis showed that late MPV (at exitus or discharged date), WBC at admission, and age increase the mortality rate 1,770, 1,202, 1,052 times, respectively.

Table 3:The receiver operating characteristic (ROC) curves and areas under the curve (AUCs) are shown

Table 4: The best cut off value based on Youden's index and the sensitivity and specificity in those criteria were calculated. In the ROC analysis, the precision of MPV measurements in predicting mortality was moderate and the area under the curve(AUC) was 0.76 (95% CI: 0.61- 0.88) with a sensitivity and specificity of 94,12% (95% CI: 71,3- 99,9) and 57,6% (95% CI: 36,9- 76,6)