The prognostic role of platelet to lymphocyte ratio and mean platelet volume in critically ill patients

A. YILDIZ[1], A. YIGIT[2], A.R. BENLI[3]

[1]Department of Hematology, Diskapi Training and Research Hospital, Ankara, Turkey, KBU Karabuk Research and Educational Hospital, Department of Internal Medicine, Karabuk, Turkey
[2]Department of Internal Medicine, KBU Karabuk Research and Educational Hospital, Karabuk, Turkey
[3]Department of Family Medicine, Karabuk University, Medical Faculty, Karabuk, Turkey

Abstract. – OBJECTIVE: The aim of this study was to identify the relationship between complete blood count parameters, mean platelet volume (MPV), and platelet to lymphocyte ratio (PLR) with mortality and hospitalization duration in critically ill patients.

PATIENTS AND METHODS: A retrospective analysis was made of patients admitted to our tertiary adult intensive Care Unit (ICU) between January 2015 and January 2016. Hemoglobin (Hb), white blood cell (WBC), lymphocyte and platelet counts were obtained from the complete blood count performed at the time of admission. MPV and PLR levels were calculated from these data. Other data were retrieved from the patient follow-up records.

RESULTS: The investigation included a total of 306 patients. The total mortality rate was 40.2%. The initial median PLR level was 206.7 (8.1-1675.0) for non-survivor patients and 194.5 (12.8-1236.6) for survivor patients. The PLR level was higher in the non-survivor group, but there was no statistically significant difference between the groups ($p>0.05$). The median MPV level was 7.66 (5.17-15.25) for the survivors and 8.09 (4.36-16.19) for the non-survivors, and there was no statistically significant difference between the groups ($p=0.237$). The median length of stay (LOS) of all patients was 7 (2-61) days. Only the Acute Physiology and Chronic Health Evaluation (APACHE) II score was found to have a positive correlation with LOS ($p<0.05$).

CONCLUSIONS: PLR has no effect on mortality rates regardless of whether the patient has thrombocytopenia or not at the time of admission. MPV levels have no significant relationship with mortality. Neither MPV nor PLR have an effect on LOS. The use of these as a prognostic factor for mortality in critically ill patients is still unclear.

Key Words:
   Platelet to lymphocyte ratio, Mean platelet volume, Critically ill patients, Mortality.

Introduction

There are many scoring systems used in the prediction of prognosis in ICU patients. Of these scoring systems, the Acute Physiology and Chronic Health Evaluation (APACHE) score measures mortality numerically using laboratory parameters together with physiological parameters that may affect mortality. It is one of the most frequently used scoring systems in ICUs[1]. In recent years, in addition to these scoring systems, different indicators have been studied which may be useful for the prediction of mortality. Hematological parameters are considered important because they are readily available and easy to interpret. With the exception of WBC and hematocrit levels, which are also included in the APACHE II score, hematological parameters which are not included in scoring systems are being investigated, such as platelet count, PLR, neutrophil to lymphocyte ratio (NLR) and MPV.

Thrombocytopenia is the most frequently seen coagulation abnormality in critically ill patients[2]. It is quite difficult to identify the reason for a decreased platelet count in ICU and it is often thought to be multifactorial[3]. Although it may differ based on how it is defined (<100000 or <150000, x 10^6/L) and the patient categories studied, thrombocytopenia prevalence and incidence in ICU patients has been reported to vary between 8.3-67.6% and 13-44% respectively[4]. In several previous reports[3-5], thrombocytopenia has been defined as an independent risk factor for mortality in ICU patients.

Regardless of the cause of admission to ICU, the increased systemic inflammatory response is evident, and it is an important cause of mortality and morbidity in critically ill patients[6]. WBC and

neutrophil count increased C-Reactive Protein (CRP) levels and, hypoalbuminemia are usually studied as biochemical parameters related to the systemic inflammatory response[7]. It has also been reported in some researches[8-11] that PLR may be used as an inflammatory marker and it is related to poor prognosis in many diseases especially cardiovascular diseases, malignancies, and chronic inflammatory diseases. In addition to PLR, NLR and its effect on intensive care mortality has become a research topic in current studies[12].

The platelet activation products that are available in circulation have a very important role in the pathogenesis of vascular and inflammatory diseases[13,14]. Mean platelet volume (MPV) is one of the factors that define thrombocyte functions[15,16]. It is a simple and cheap test which is routinely measured, and easy to interpret. It has been previously reported that MPV is increased in diseases such as diabetes mellitus, myocardial infarction, and hyperthyroidism. Moreover, MPV has prognostic value in some other diseases[16].

The aim of this study was to present the results of the analysis of the effect of complete blood count parameters, PLR, MPV and APACHE II score on mortality and length of stay (LOS) of patients admitted to the Internal Medicine Adult ICU of Karabuk University Training and Research Hospital.

Patients and Methods

Patients

A retrospective analysis was made of patients admitted to The Medical ICU of Karabuk University Training and Research Hospital from January 2015 to January 2016. The study included a total of 306 patients who were followed up for at least 48 hours. Patients with a length of stay (LOS) of less than 48 hours, with hematological malignancies or who were admitted to ICU because of a surgical diagnosis were excluded from the investigation.

The evaluation was made of the demographic information, laboratory test results, APACHE II scores, diagnosis at the time of admission, LOS in ICU and mortality rate of the patients by reviewing the medical records and hospital database. In our ICU, CBC is performed daily as part of routine care. A blood sample for CBC was collected into a tube containing ethylenediaminetetraacetic acid (EDTA). In our institution, the mean time between the drawing of blood samples and the start of sample processing is approximately 30 minutes. The WBC count (x 10^6/L), lymphocyte count (10^6/L), platelet count (x 10^6/L), Hb level (g/dl) and MPV were recorded. The PLR value was calculated using these measurements. According to our hospital biochemistry laboratory database, normal platelet level range is 140000-450000 (x 10^6/L). For the analyses, the studied population was separated into 2 groups as survivors and non-survivors. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval for this study was granted by the Local Ethics Committee (date: 02.11.2016, approval number: 8).

Statistical Analysis

SPSS Statistics 19 software (IBM, Armonk, NY, USA) was used for statistical analysis. In the comparison of variables distributed homogeneously, the t-test was used for parametric variables and the x^2-test was used for non-parametric variables. For variables not showing homogeneous distribution, the Mann Whitney U-test was used. Data were expressed as mean ± standard deviation (SD) and median (minimum-maximum) values. Multiple logistic regression analyses were used to determine the risk factors for mortality and LOS. $p < 0.05$ was accepted as statistically significant.

Results

A total of 306 patients included 141 males (46%) and 165 females (54%) with a mean age of 74.4 ±12.3 years; 73.2 ±12.5 years for male patients and 75.5 ±12.17 years for female patients. A total of 123 (40.2%) patients, 57 male and 66 female, died during the follow-up period and 183 (59.8%) patients, 84 male and 99 female, survived and were either transferred to other departments in the hospital or discharged. The demographic data are shown in Table I. The route to ICU showed that 158 patients were accepted from the Emergency Dept (51.6%), 90 patients from other departments of the hospital (29%), the remainder came from other ICUs and external medical centers. The most common diagnoses for ICU admission were acute respiratory failure (18.6%), sepsis (16.3%) and pneumonia (13.7%). The reasons for ICU admission are shown in Table II.

Table I. Baseline characteristics of patients.

	Male	Female	All
Age (SD)	73.24 (± 12.5)	75.52 (± 12.17)	74.4 (±12.3)
Non-survivor (no.)	57	66	123
Survivor (no.)	84	99	183
LOS (days, median)	7 (2-44)	7 (2-61)	7 (2-61)
No.	141	165	306

LOS: Length of stay, SD: Standard deviation.

Table II. Causes of ICU admission.

Diagnosis	All (no.=306), n (%)
Acute respiratory failure	57 (18.6)
Sepsis	50 (16.3)
Pneumonia	42 (13.7)
Acute COPD exacerbation	24 (7.8)
Gastrointestinal bleeding	21 (6.8)
Others	112 (36.8)

COPD: Chronic Obstructive Pulmonary Disease.

The median APACHE II score of the whole patient group was 25 (3-47). It was significantly higher in non-survivors than survivors (31 *vs*. 20; *p*=0.00). When the CBC at the time of admission was examined, the average Hb level was 11.1 g/dl (± 2.4), median WBC count was 12590 (265-47010) (×10^6/L), median platelet count was 253725 (8500-970200) (×10^6/L) and median MPV level was 7.8 (4.3-16.1). The median PLR was found to be 198.8 (8.1-1675.0).

When the relationship between hematological parameters and mortality was examined, Hb level and platelet count were found to be similar in both the survivor and non-survivor groups (*p*>0.05). The WBC count of non-survivors was significantly higher than that of survivors (*p*=0.01). (Table III). The median MPV level was 8.09 (4.3-16.1) for non-survivors and 7.6 (5.1-15.2) for survivors with no significant difference determined (*p*=0.23). The median PLR level was 206.7 (8.1-1675) for non-survivors, which was higher than that of survivors 194.5 (12.8-1236.6), but not statistically significant (*p*=0.63). All these parameters and the relationships with mortality are shown in Table III.

A positive correlation was determined between WBC and platelet count, and between PLR and platelet count. PLR didn't correlate with any other parameters except platelet count. A negative correlation was determined between MPV level and platelet count and PLR. The correlation table of the hematological parameters is shown in Figure 1.

The mortality rate of the patients with thrombocytopenia (platelet<140000 x10^6/L) at the time

Table III. Hematological parameters, APACHEII score, PLR and MPV levels and their relationship with mortality.

	All patients	Non-survivors	Survivors	
Parameters	All (no.: 306), average (± SD), Median (range)	All (no.: 123), average (± SD), Median (range)	All (no.: 183), average (± SD), Median (range)	p
APACHE II	25 (3-47)	31 (12-47)	20 (3-41)	0.00
Hb (g/dl)	11.1 (±2.4)	11.0 (±2.4)	11.1 (±2.5)	0.10
WBC (×10^6/L)	12590 (265-47010)	13440 (265-40990)	11250 (948-47010)	0.01
Plt (×10^6/L)	253725 (8500-970200)	245800 (8500-970200)	258900 (15060-835300)	0.08
MPV	7,87 (4.36-16.19)	8.09 (4.36-16.19)	7.66 (5.17-15.25)	0.23
PLR	198.8 (8.1-1675.0))	206.7 (8.1-1675.0)	194.5 (12.8-1236.6)	0.63

APACHE: Acute physiology and chronic health evaluation, Hb: Hemoglobin, WBC: White blood cell, Plt: Platelet, MPV: Mean platelet volume, PLR: Platelet to lymphocyte ratio.

Table IV. The relation of platelet count at the time of admission with mortality and PLR.

	Platelet count at the time of admission		
	Normal (no. = 231)	Thrombocytopenia (no. = 75)	*P*
Survivors (no.)	146	37	
Non-survivors (no.)	85	38	
Mortality rates (%)	36.7	50.6	0.03
PLR	226 (16.8-1675)	134.5 (8.1-697.3)	0.00

PLR: Platelet to lymphocyte ratio.

of admission was higher than that of patients with a normal thrombocyte count (50.6% *vs.* 36.7%, *p*=0.03). The median PLR level of the patients admitted with thrombocytopenia was significantly lower than that of patients with a normal platelet count (134.5 (8.1-697.3) *vs.* 226 (16.8-1675), *p*=0.00). The correlations of platelet count at the time of admission with mortality and PLR are shown in Table IV. In patients with a normal thrombocyte count, the median PLR was slightly higher in the non-survivor group but not statistically significant (*p*=0.17).

From the APACHE II, thrombocytopenia, WBC count, Hb level, MPV and PLR values, multiple logistic regression analysis was applied to the APACHE II, thrombocytopenia and WBC count due to their significant relationship with mortality. APACHE II and thrombocytopenia were left on the model with a value of *p*<0.15. According to the result of this analysis, the odds ratio of APACHE II score for mortality was found

to be 1.187 (95% Confidence Interval), and the odds ratio of thrombocytopenia for mortality was found to be 1.858 (95% Confidence Interval).

When the relationship between the hematological parameters and LOS was analyzed, there was no significant relationship of Hb levels, WBC count, platelet count, thrombocytopenia at the time of admission, MPV and PLR levels with LOS. A positive correlation was only determined between the APACHE II score and LOS (*p*=0.01). All hematological parameters and their correlation with LOS are shown in Figure 1.

Discussion

Many studies have examined the factors affecting mortality and the risk scoring methods in intensive care patients. Although there are several scoring systems, the APACHE II score is still one of the most frequently used risk scoring systems
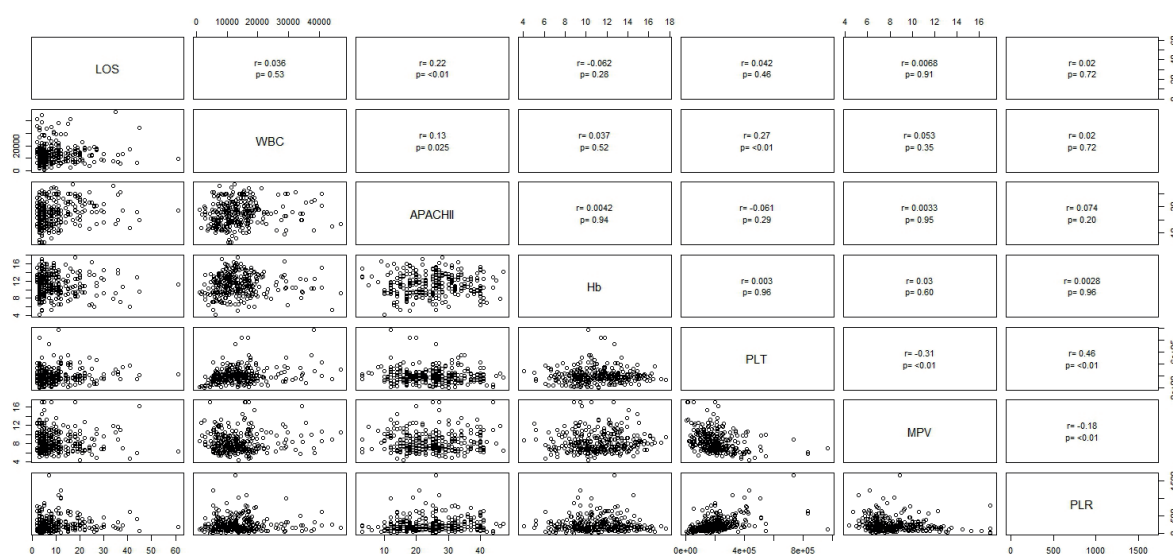

Figure 1. The correlation of CBC parameters, APACHE II score, PLR, MPV and Length of Stay (LOS).

as physiological, hematological and biochemical parameters are evaluated together and it has high success rate for the prediction of mortality. In the current work, the APACHE II score was determined to have a significantly positive correlation with both mortality and LOS. In a previous study[17], the APACHE II score was reported to be a strong predictor of mortality in critically ill patients but not adequate for predicting LOS. Therefore, in recent years, in addition to these scoring systems, different indicators such as hematological parameters and some biochemical markers have been studied to determine whether they have any effect on predicting mortality and LOS. In this investigation, an analysis was made of the relationships of Hb level, WBC count, platelet count, MPV and PLR levels with mortality and LOS. Thrombocytopenia at the time of ICU admission has been proven in many recent studies[3,5,18] to be one of the most significant and independent risk factors for mortality in critically ill patients. In a cohort study in 2013, Williamson et al[18] reported that both thrombocytopenia at the time of admission and the development of thrombocytopenia during the follow-up period were independent risk factors for mortality and LOS in 20696 patients admitted to internal medicine, surgery and cardiovascular ICUs. This effect on mortality and LOS was found to be more significant in patients admitted with genitourinary, gastrointestinal, respiratory, vascular and infectious causes.

In the current study, the median platelet count was found to be similar in both the survivor and non-survivor groups. However, a higher mortality rate was seen in patients with thrombocytopenia at the time of admission than in patients with no thrombocytopenia, which was consistent with literature. The odds ratio of thrombocytopenia for mortality was 1.85.

Platelet activation in inflammation and infection, and also during thrombosis and bleeding conditions, and thrombocytopenia is a risk factor for mortality[13,14]. Therefore, the effect of MPV on mortality and LOS is one of the other parameters newly focused on. Conflicting results have been reported in respect of the effect of MPV on mortality. In the first report on this subject, Zhang et al[19] showed that a higher MPV level is a significant risk factor for higher mortality in critically ill patients. Similarly, in another work[20], MPV was found to be higher in non-survivor patients than survivors and there was a positive correlation with mortality rates. In contrast, another study[21] showed no effect of MPV on mortality in critical-

ly ill patients. In the current study, a higher MPV value was determined in non-survivors than in survivors but it was not statistically significant. Due to these conflicting results, it is still not possible to make a definitive conclusion about the effect of MPV on mortality.

It has been shown that PLR is related to poor prognosis in many diseases, especially cardiovascular diseases, malignancies, and chronic inflammatory diseases[8-11]. To the best of our knowledge, there are two reports which have analyzed the relationship between PLR and mortality in critically ill patients. In the first study[22], it was reported that a higher PLR presents a higher risk for re-admission and mortality in critically ill patients with diabetic ketoacidosis. In the second study, Kutlucan et al[20] found higher PLR levels in a non-survivor group compared to patients who survived but the difference was not statistically significant. In the current study, despite the largest patient number about this topic in literature, similar results were obtained that PLR in non-survivors was higher than in survivors but not to a statistically significant level. This could have been due to the presence of thrombocytopenia at the time of admission, because thrombocytopenia is one of the most significant risk factors of mortality. Furthermore, significantly lower PLR values were observed in patients with thrombocytopenia than in patients with a normal platelet count. In other words, mortality was higher in thrombocytopenic patients while PLR was lower. Therefore, thrombocytopenia may inhibit the PLR increase, which is expected in non-survivor patients. Accordingly, PLR levels were analyzed only in patients with a normal platelet count at the time of admission and PLR was compared between the survivors and non-survivors of these patients. In the analysis, a higher PLR was observed in non-survivors than in survivors but again it was not statistically significant, similar to the result of the whole patient group. Consequently, there was no significant relationship between PLR and mortality rate regardless of whether the patient had thrombocytopenia or not at the time of admission. It can be considered that larger patient population-based studies are needed to obtain a significant relationship.

There have also been investigations about the relationship between hematological parameters and LOS. It has been previously reported[18] that thrombocytopenia increases the risk of both mortality and LOS. In contrast, in the current investigation, no relationship was determined between LOS and thrombocytopenia at the time of admis-

sion. In a recent study[20], there was a positive correlation of LOS with PLR but not with Hb level, platelet count, WBC count and MPV. Another report[21] revealed that MPV has no effect on LOS in critically ill patients. When the relationship between all hematological parameters with LOS was analyzed, no significant relationship was determined in our study. Only the APACHE II score was correlated with LOS positively (Figure 1).

Conclusions

Many parameters are used to predict prognosis in ICU patients. Of these, CBC parameters play an important role but recently investigators have highlighted the effect of PLR and MPV on prognosis in critically ill patients. We showed that the mortality rates were significantly higher in patients who have thrombocytopenia at the time of admission and higher APACHE II scores. Although MPV levels were higher in the non-survivor group, there was no effect on mortality and LOS. There was no significant relationship between PLR and mortality rate and LOS regardless of whether the patient had thrombocytopenia or not at the time of admission. As there are conflicting results in literature as to whether PLR and MPV are significant risk factors for mortality and LOS, it is not appropriate to use them as prognostic factors in critically ill patients.

Conflict of Interest

The author(s) declare that they have no substantial direct or indirect commercial financial incentive associated with publishing the article.

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