The Prognostic Role of Mean Platelet Volume (MPV) in Sever Sepsis: is it True?

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ARTICLE INFO

Article type:
Original Article

Abstract

Background: The purpose of the present study was to examine the role of mean platelet volume (MPV) in comparison with Sequential Organ Failure Assessment (SOFA), quick SOFA (qSOFA), and Mortality in Severe Sepsis in the Emergency Department (MISSED) scoring systems in predicting hospital mortality among patients with severe sepsis.

Methods: This follow-up study was conducted on patients over 18 years with severe sepsis, who were referred to the emergency department. Complete blood count (CBC) samples were sent to the laboratory for MPV measurement. Also, the required samples for determining SOFA and MISSED scores were collected. A senior emergency medicine resident completed the questionnaires upon patient admission and during follow-ups. Hospital mortality was considered as the outcome of the study. All statistical analyses were performed using SPSS version 20.

Results: Among 428 patients with severe sepsis, 200 cases were recruited in this study from May 1, 2017, to May 1, 2018. The frequency of hospital mortality was 56 (28%). In the univariate analysis, there was a significant relationship between hospital mortality and age, base excess (BE), MPV, platelet distribution width (PDW), SOFA score, qSOFA score, and MISSED score (P< 0.0001). Based on the backward conditional method in the multivariate analysis, three variables, including SOFA, qSOFA, and MISSED scores, which showed a significant relationship with hospital mortality, remained in the final model.

Conclusion: It seems that MPV plays a less significant role in determining the outcomes of severe sepsis in patients. qSOFA and MISSED scores, especially SOFA score, are of great significance in determining the prognosis of these patients.

Citation: Chalabi A.H, Torabi M, Mirzaee M. The Prognostic Role of Mean Platelet Volume (MPV) in Sever Sepsis: is it True?. *Journal of Kerman University of Medical Sciences*, 2019; 26 (2): 136-144.

Introduction

Sepsis is described as a physiological-pathological syndrome, associated with biochemical abnormalities induced by infection. Considering the high rate of mortality in septic patients, this condition has become a major healthcare problem. Despite major advances in medical sciences, the number of hospitalized septic patients is increasing worldwide; therefore, rapid diagnosis and prognosis of these patients are of great significance (1-3).

For almost two decades, the systemic inflammatory response syndrome (SIRS) criteria have been applied in

the diagnosis of sepsis. These diagnostic criteria include: body temperature $< 36°C$ or $> 38°C$; heart rate > 90 beats per minute; respiratory rate > 20 breaths per minute; white blood cell count $< 12\,000$ mL^3 or < 4000 mL^3; and presence of immature neutrophils (bands) $> 10\%$. Generally, sepsis is described by the presence of SIRS, associated with infection or possible infection. Diagnosis of sepsis is currently based on the modified Sepsis-3 definition, which characterizes sepsis by organ dysfunction and an increase of two points (or more) in the total Sequential Organ Failure Assessment (SOFA) score.

Since SOFA involves the measurement of laboratory tests, quick SOFA (qSOFA) can be applied for septic patients given the simplicity of measurements. This system encompasses respiratory rate, systolic blood pressure, and Glasgow coma scale (GCS) score. Respiratory rate ≥ 22 breaths/min, systolic blood pressure ≤ 100 mmHg, and altered mental status characterize sepsis in this scoring system; these criteria can be taken into account for determining the prognosis of hospitalized septic patients (3-5).

Mortality in Severe Sepsis in the Emergency Department (MISSED) score is also a prognostic system of mortality in septic patients, which consists of three independent variables: age ≥ 65 years; albumin < 2.7 g/dL; and international normalized ratio (INR) > 1.2. A MISSED score above 5.5 is indicative of an increased risk of mortality in septic patients (6, 7).

In addition, there are laboratory tests, besides these scoring systems, which can have predictive values in severe sepsis. One of these tests is the mean platelet volume (MPV), which represents the size, function, and activity of platelets and varies relative to the extent and severity of inflammation. Considering the increased use of large platelets and presence of smaller platelets in blood circulation, increased inflammation is associated with reduced MPV; on the other hand, lower inflammation indicates a higher MPV. This simple laboratory test seems to be prognostically valuable in severe cases, although there are discrepancies in the literature (8-10).

Objectives

Considering the high incidence and mortality of sepsis in hospitals, this study investigated the role of MPV in comparison with SOFA, qSOFA, and MISSED scores in predicting the mortality of patients with severe sepsis, referred to the emergency department. We aimed to reduce mortality through prompt diagnosis of severe cases and rapid initiation of treatment.

Materials and Methods
Study design

This follow-up study was performed on patients (age > 18 years) with severe sepsis, who were referred to the Emergency Department of Afzalipur Hospital (a referral center for internal and infectious diseases) in Southeast of Kerman, Iran. The patients were required to meet at least two SIRS criteria; they also had an infection or a possible infection and showed at least one organ dysfunction. On the other hand, septic patients, who did not have any organ dysfunctions during the study, were excluded. Other exclusion criteria were as follows:

chronic lung disease; diabetes; treatment with corticosteroids, nonsteroidal antiinflammatory drugs (NSAIDs), angiotensin converting enzyme (ACE) inhibitors, and statins; history of antiplatelet or anticoagulant therapy in the past two weeks; systemic hypertension; heart failure; anemia; deep vein thrombosis; pulmonary embolism; malignancies; pregnancy; rheumatic disorders; age < 18 years; and unwillingness to cooperate.

This study was approved by the Ethics Committee of Kerman University of Medical Sciences [IR.KMU.REC.1397.090]. Oral consents were also obtained from all the patients before inclusion in the study.

Patient sample

A total of 200 patients, who met the inclusion criteria, were enrolled in this study from May 1, 2017 to May 1, 2018.

Blood samples and measurements

Upon the admission of patients to the emergency department, their baseline vital signs were measured, and variables including age, sex, and mental status were recorded. Within one hour after admission, complete blood count (CBC) samples were sent to the laboratory for MPV measurements, while arterial blood gas (ABG) samples were sent for base excess (BE) assessments. Also, the required samples were collected to determine SOFA and MISSED scores. Questionnaires were completed by a senior emergency medicine resident at baseline and during follow-ups. Hospital mortality was considered as the outcome of the study. Finally, the association of hospital mortality with MPV, SOFA, qSOFA, and MISSED scores was examined.

Statistical analysis

Mean (±SD) was measured for describing quantitative variables, while frequency percentage was calculated for qualitative variables. The odds ratio (OR) and 95% confidence interval (CI) were used for expressing the significance of associations. *P*-value less than 0.05 was considered statistically significant in all statistical tests. First, a univariate analysis was conducted, and then, for variables with *P*< 0.25, multivariate analysis was carried out using a logistic regression model to determine significant associations (*P*< 0.05) (11). Finally, the ROC curve was plotted for variables with a significant relationship with the study outcome. All statistical analyses were performed using SPSS version 20.

Results

Of 428 patients with severe sepsis, who were referred to the emergency department, 228 were excluded and 200 were enrolled (Figure 1). The frequency of hospital mortality was 56 (28%). The mean age of the patients was 68.13±15.34 years. A total of 105 (52.5%) men and 95 (47.5%) women were included in the study (Table 1). In the univariate analysis, there was a significant relationship between hospital mortality and age, BE, MPV, platelet distribution width (PDW), SOFA score, qSOFA score, and MISSED score (*P*< 0.0001). On the other hand, there was no significant relationship between sex and outcome (*P*= 0.28) (Table 2).
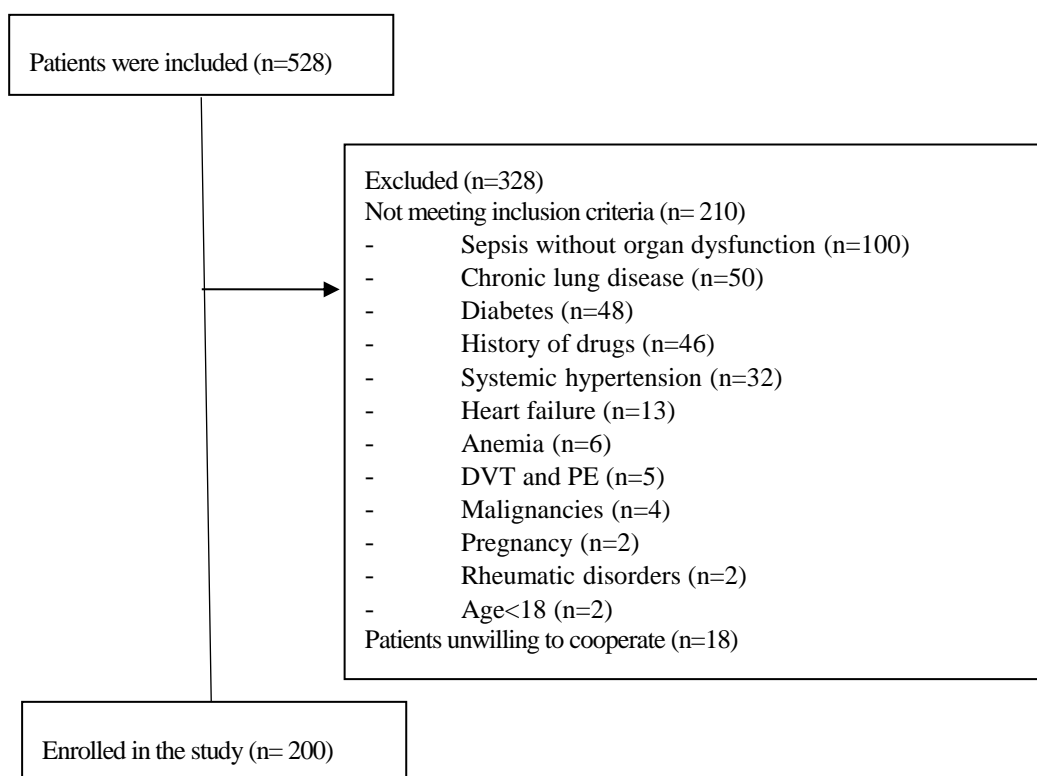
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│ Patients were included (n=528) │
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Excluded (n=328)
Not meeting inclusion criteria (n= 210)
-      Sepsis without organ dysfunction (n=100)
-      Chronic lung disease (n=50)
-      Diabetes (n=48)
-      History of drugs (n=46)
-      Systemic hypertension (n=32)
-      Heart failure (n=13)
-      Anemia (n=6)
-      DVT and PE (n=5)
-      Malignancies (n=4)
-      Pregnancy (n=2)
-      Rheumatic disorders (n=2)
-      Age<18 (n=2)
Patients unwilling to cooperate (n=18)

Enrolled in the study (n= 200)

Figure 1. Flow chart showing enrollment of patients

Table 1. Baseline characteristics

Variables	N (%)
Age (years), mean ± SD	68.13±15.34
Gender	
Male	105 (52.5)
Female	95 (47.5)
BE (meq/lit), mean ± SD	0.80±4.10
MPV (fL), mean ± SD	9.45±1.03
PDW (fL), mean ± SD	11.78±1.89
SOFA, mean ± SD	4.27±2.42
qSOFA, mean ± SD	0.98±0.82
Missed score, mean ± SD	3.38±2.62
Hospital mortality	56 (28)

Abbreviations: BE, Base excess; MPV, Mean platelete volume, PDW, Platelet distribution width; SOFA, Sequential Organ Failure Assessment; qSOFA, quick Sequential Organ Failure Assessment; Missed, Mortality in Severe Sepsis in the ED.

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Table 2. Associations with predicting hospital mortality using univariate regression analysis

Variables	Mortality (mean± SD)		OR(95% CI)	P-Value
	Yes	No		
Age	76.16±14.78	65.00±14.44	1.06(1.03-1.09)	<0.0001
BE	-1.69±4.60	1.77±3.45	0.79(0.72-0.87)	<0.0001
MPV	10.23±0.90	9.15±0.91	3.47(2.28-5.26)	<0.0001
PDW	13.18±1.79	11.24±1.63	1.94(1.53-2.45)	<0.0001
SOFA	6.95±2.17	3.22±1.56	3.15(2.23-4.45)	<0.0001
qSOFA	1.76±0.76	0.68±0.63	8.79(4.65-16.60)	<0.0001
Missed score	6.16±2.09	2.29±1.91	2.45(1.91-3.14)	<0.0001

Variables with $P < 0.25$ were entered in the multivariate analysis. Using the backward conditional method, three variables, including SOFA, qSOFA, and MISSED scores, which showed significant associations with hospital mortality, remained in the final model (Table 3). For variables with a significant relationship with hospital mortality, the ROC curve was plotted, and the area under ROC curve (AUC) was calculated. The largest areas were attributed to SOFA, qSOFA, and MISSED scores (0.92, 0.84, and 0.89, respectively) (Table 3; Figures 2-4).

Figure 2. Receiver operating characteristic curve for SOFA predicting hospital mortality.

Table 3. Associations with predicting hospital mortality using multivariate regression analysis

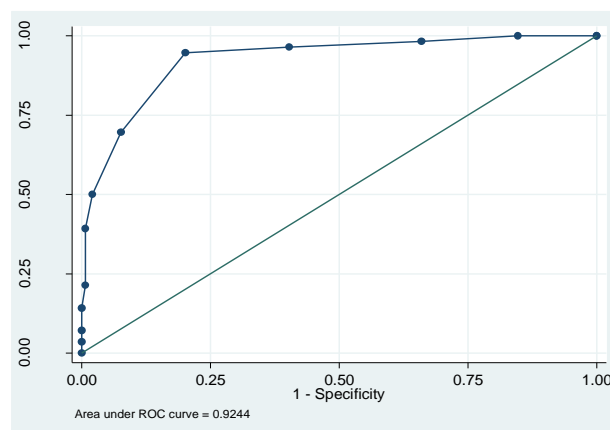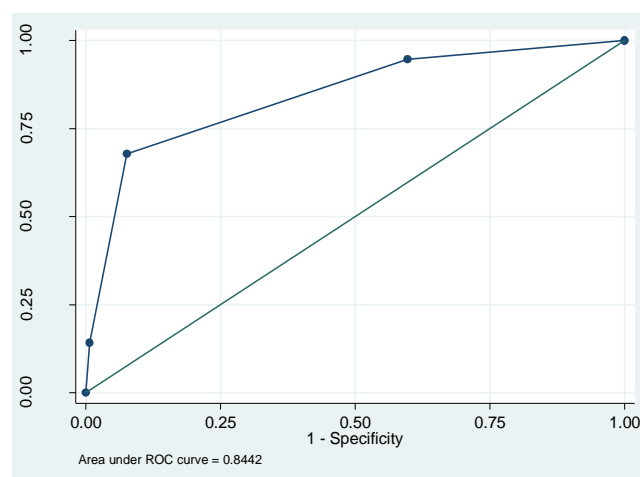| Variables	OR(95% CI)	P-Value	ROC curve
SOFA	2.23(1.49-3.33)	0.017	0.92
qSOFA	2.27(1.04-4.94)	<0.0001	0.84
Missed score	1.80(1.35-2.40)	<0.003	0.89

Figure 3. Receiver operating characteristic curve for qSOFA predicting hospital mortality.
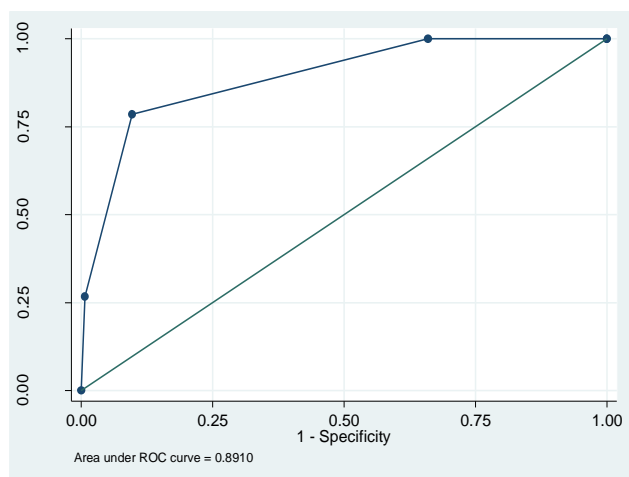
Figure 4. Receiver operating characteristic curve for Missed score predicting mortality.

Discussion

Considering the high rate of mortality in septic patients, prognostic assessment is of great importance. The present findings indicated the insignificant prognostic role of MPV in determining the mortality of patients with severe sepsis. In these patients, multiparameter scoring systems, such as SOFA, qSOFA, and MISSED scores, can be used to determine prognosis in emergency departments.

Several studies have investigated the role and changes of MPV in inflammatory, infectious, and thrombotic diseases; however, the results are contradictory in the literature. MPV is expected to increase in the event of mild inflammation and thrombosis, while it decreases in case of severe inflammation (8). According to the literature, an increase of MPV in septic patients is directly related to the severity of the disease. Besides determining the severity of sepsis, MPV can be used to predict the prognosis of patients; in other words, a higher MPV is expected to indicate the greater severity of the disease and poorer prognosis (10). In this regard, a study

by Zampieri et al. revealed that hospital mortality is associated with an increase in MPV within 24 hours after hospitalization (12); even MPV changes from baseline is associated with mortality in patients with severe sepsis or septic (13). However, contradictory results have been reported regarding the association of MPV with the prognosis of septic patients. Oh GH et al. in a study on septic patients showed that MPV at baseline had no prognostic value (14). Similarly, in a study by Tajarernmuang et al., initial screening of this laboratory test at baseline showed no prognostic importance in critically ill patients (9). Our study also showed that MPV measurement at baseline is not helpful in determining the mortality of patients referred to the emergency department.

Multivariate systems play an important role in determining the prognosis of septic patients in intensive care units. The SOFA system includes several parameters and examines several vital organs, including the heart, brain, kidneys, lungs, and liver. Assessment of most of these organs, which is based on laboratory tests, increases the validity of SOFA system (versus SIRS and qSOFA systems) in predicting the mortality of septic patients and supports its application in patients with clinical sepsis features (15). However, sepsis diagnosis based on SOFA criteria is usually delayed, as different tests need to be administered (16). Nonetheless, this system may be helpful in predicting mortality in septic patients. In other words, higher SOFA scores indicate a higher risk of mortality in patients (17, 18), as confirmed in our study.

The qSOFA system, which involves the assessment of vital signs, is a simple and quick index. This system examines respiratory rate, mental state, and systolic blood pressure and may play a role in the prediction of

mortality in septic patients. In other studies, the prognostic accuracy of qSOFA for hospital mortality was higher than that of SIRS in patients with suspected sepsis referred to the emergency department (19, 20). On the other hand, qSOFA has been shown to have high specificity and moderate sensitivity in predicting mortality; accordingly, it is considered as a poor screening tool for sepsis. In fact, the single-purpose application of this system for diagnosis can lead to delayed treatment and subsequently result in the poor prognosis of these patients (21, 22). In a study by Wang et al. the prognostic value of qSOFA was found to be equal to SOFA in predicting mortality (23). Given its simplicity, this system can be a proper guide for predicting mortality in septic patients at emergency departments. Similarly, our study showed that qSOFA can be helpful in identifying the prognosis of patients with severe sepsis. In addition, it is an applicable system in emergency departments considering the simplicity of its parameters.

The MISSED scoring system consists of three independent variables, including age, albumin level, and INR, with a prognostic value equivalent to APACHE II score. Sivayoham et al. in two articles showed that this scoring system could help determine the prognosis of severe sepsis in patients. It can be also applied in emergency departments to identify septic patients, who are at a high risk of mortality (24, 25). In addition, a study by McCormack et al. confirmed the effectiveness of this system in predicting hospital mortality; in fact, given the high admission rate of emergency departments, the

simplicity of this prognostic system is an advantage (26). The present study also reported that this scoring system could help determine the prognosis of septic patients.

There are several limitations in the present study. One of these limitations was its single-center design; however, the significance of this shortcoming was diminished, as the examined hospital was a referral center and our study had a prospective design. In addition, a large number of patients were eliminated from this study based on the exclusion criteria (lack of organ involvement; pregnancy; age < 18 years; and chronic, inflammatory, or thrombotic diseases). Also, it was not possible to conduct lactate tests or consistent albumin tests during the day. Finally, patients who were unwilling to cooperate were excluded from the study.

Conclusion

It seems that MPV measurement, in comparison with multivariable scoring systems, plays an insignificant role in determining the outcomes of patients with severe sepsis in emergency departments. Overall, qSOFA and MISSED scoring systems, especially SOFA score, are of great significance in predicting the prognosis of patients with severe sepsis. In addition, qSOFA and MISSED scores as simple scoring systems can be proper and rapid guides for emergency physicians to determine the prognosis of severe sepsis in patients.

Conflict of interest

None declared.

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