Journal of Critical Care 29 (2014) 885.e1–885.e6

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Platelet indices are novel predictors of hospital mortality in intensive care unit patients☆

Zhongheng Zhang, MM*, Xiao Xu, MB, Hongying Ni, MM, Hongsheng Deng, MM

Department of critical care medicine, Jinhua municipal central hospital, Zhejiang, PR China

ARTICLE INFO

Keywords:
Platelet distribution width
Intensive care unit
Mortality
Mean platelet volume

ABSTRACT

Background and objective: Platelet volume indices (PVIs) are inexpensive and readily available in intensive care units (ICUs). However, their association with mortality has never been investigated in a critical care setting. Our study aimed to investigate the association of PVI and mortality in unselected ICU patients.
Methods: This was a retrospective study conducted in a mixed 24-bed ICU from September 2010 to December 2012. Platelet indices including mean platelet volume (MPV), platelet distribution width (PDW), platelet count, and plateletcrit were measured on ICU entry. Univariable analyses were performed to screen for variables that were associated with mortality. Variables with $P < .1$ were incorporated into a regression model to adjust for the odds ratio of platelet indices.
Results: A total of 1556 patients were included during the study period, including 1113 survivors and 443 nonsurvivors (mortality rate: 28.47%). Platelet distribution width and MPV were significantly higher in nonsurvivors than in survivors. Platelet distribution width greater than 17% and MPV greater than 11.3 fL were independent risk factors for mortality (adjusted odds ratio: 1.92 and 1.84, respectively) and survival time (hazards ratio: 1.77 and 1.75, respectively).
Conclusion: Higher MPV and PDW are associated with increased risk of death, whereas the decrease in plateletcrit is associated with increased mortality risk.

1. Introduction

Platelet volume indices (PVIs) are a group of platelet parameters that can be routinely obtained in complete blood count by many automated analyzers. The most commonly measured PVI includes mean platelet volume (MPV) and platelet distribution width (PDW). Mean platelet volume is the ratio of plateletcrit to platelet count and is measured in femtoliters. *Platelet distribution width* is defined as the distribution width at the level of 20% in platelet size distribution curve [1]. Platelet volume indices are biomarkers of platelet activation that are thought to be associated with systemic inflammatory responses [2–4]. They are inexpensive and readily available in many institutions, allowing for extensive clinical investigations focusing on the diagnostic and prognostic values of PVIs in varieties of settings. In hematology, for instance, they are used for the differential diagnosis of thrombocytopenia and thrombolysis [5,6].

In cardiovascular disease, they are regarded as a risk factor for myocardial infarction (MI) and post-MI mortality [7,8]. Platelet volume indices are potential biomarkers of platelet activity, with higher MPV suggesting greater prothrombotic states [9]. The latter condition has been associated with adverse outcomes in critical illness. For instance, the underlying mechanism of multiple organ failure in sepsis is partly attributable to widespread thrombosis in the microcirculation [10]. However, to the best of our knowledge, PVIs have never been investigated in the intensive care unit (ICU) setting. Patients in the ICU are at significantly increased risk of death, and risk stratification is of paramount importance that it can better inform clinicians and family members of the clinical outcome. Furthermore, by establishing the linkage between PVI and clinical outcome, we can get additional insights into common pathways of critical illness. Therefore, we aimed to investigate the association of PVIs and clinical outcomes in ICU patients. We hypothesized that PVIs, including PDW and MPV, were independently associated with mortality in unselected ICU patients.

2. Patients and methods

This was a retrospective study conducted in a tertiary 24-bed ICU of an academic teaching hospital. Our department was a mixed central ICU enrolling medical, surgical, neurosurgical, and cardiopulmonary bypass surgery patients. The study included patients admitted to the ICU between September 2010 and December 2012. Patients' information including demographics, hospital admission and discharge dates, diagnosis, physiological signs, medication, and fluid balance were stored electronically in the Haitai medical system (Haitai Medical

☆ Conflict of interests: The authors declare that they have no competing interests.

* Corresponding author. 351#, Mingyue Rd, Jinhua, Zhejiang province, China, 321000. Tel.: +86 579 8255 2667.
E-mail address: zh_zhang1984@hotmail.com (Z. Zhang).

http://dx.doi.org/10.1016/j.jcrc.2014.04.020
0883-9441/

Table 1
Comparison of demographic and clinical variables between survivors and nonsurvivors

Variables	Total (N = 1556)	Survivors (n = 1113)	Nonsurvivors (n = 443)	*P*
Sex (male, %)	1021 (65.62)	714 (64.15)	307 (69.30)	.054
Age (y)	61.4 ± 19.3	60.7 ± 19.0	63.1 ± 20.0	.029
Charlson index (median, IQR)	1 (0, 2)	0 (0, 2)	2 (0, 3)	<.001
Blood transfusion	351 (22.6)	216 (19.4)	135 (30.5)	<.001
PRBC	334 (21.5)	207 (18.6)	127 (28.7)	<.001
FFP	344 (22.1)	209 (18.8)	135 (30.5)	<.001
Platelet	216 (13.9)	120 (10.8)	96 (21.7)	<.001
Primary diagnosis (n, %)				<.001
Pulmonary	254 (16.32)	170 (15.27)	84 (18.96)	
Cardiovascular	311 (19.99)	253 (22.73)	58 (13.09)	
Trauma	185 (11.89)	158 (14.20)	27 (6.09)	
Neurosurgical	321 (20.63)	205 (18.42)	116 (26.19)	
Post-CPR	14 (0.90)	2 (0.18)	12 (2.71)	
Multiorgan failure	19 (1.22)	9 (0.81)	10 (2.26)	
Pancreatitis	23 (1.48)	14 (1.26)	9 (2.03)	
Abdominal	166 (10.67)	122 (10.96)	44 (9.93)	
Shock	103 (6.62)	72 (6.47)	31 (7.00)	
OB/Gy	36 (2.31)	18 (1.62)	18 (4.06)	
Urinary	17 (1.09)	15 (1.35)	2 (0.45)	
Unclassified	107 (6.88)	75 (6.74)	32 (7.22)	
Laboratory parameters on ICU entry				
PDW (%)	13.9 ± 3.1	13.7 ± 3.0	14.4 ± 3.3	<.001
<9	55 (4.12)	44 (4.45)	11 (3.16)	.297
>17	220 (14.66)	125 (11.69)	95 (21.99)	<.001
Platelet count ($\times 10^3/\mu L$)	186.8 ± 125.4	203.4 ± 131.1	145.3 ± 98.6	<.001
<100	364 (27.35)	201 (21.82)	163 (39.76)	<.001
>300	225 (18.88)	192 (21.05)	33 (11.79)	.001
MPV (fL)	10.7 ± 1.4	10.5 ± 1.4	11.1 ± 1.4	<.001
<7.7	7 (0.65)	6 (0.74)	1 (0.38)	.536
>11.3	485 (31.31)	302 (27.28)	183 (41.40)	<.001
Plateletcrit	0.196 ± 0.107	0.210 ± 0.108	0.160 ± 0.094	<.001
Albumin (g/L)	30.3 ± 6.7	31.3 ± 6.3	28.3 ± 7.3	<.001
RDW (%)	14.4 ± 2.0	14.2 ± 1.9	14.9 ± 2.1	<.001
WBC ($\times 10^3/\mu L$)	12.1 ± 22.4	11.0 ± 5.8	14.9 ± 40.9	.0024
Hemoglobin (g/l)	106.4 ± 23.5	107.8 ± 22.7	102.7 ± 25.0	<.001

PRBC indicates packed red blood cell; FFP, fresh frozen plasma; CPR, cardiopulmonary resuscitation; IQR, interquartile range.

Information Systems Co, Ltd, Nanjing, PR China). Patients were excluded if (1) they stayed in the ICU for less than 24 hours, (2) PVIs were not obtained, (3) they or their family members signed the do-not-resuscitate order, or (4) they transferred to other hospitals for further treatment (denoted as automatically discharged in the Haitai medical system). The study was approved by institutional review board of our hospital, and informed consent was waived because of the retrospective nature of the study.

Abstracted data included demographics, hospital admission/discharge date, date of death and ICU discharge, the primary diagnosis on admission (reasons for ICU admission), use of mechanical ventilation and renal replacement therapy, the Charlson comorbidity index, and blood transfusions both in the emergency department and in the ICU. Laboratory parameters including platelet count, PDW, MPV, plateletcrit, albumin, red cell distribution width (RDW), white blood cell count (WBC), and hemoglobin were collected. Because we used a medical information system that could only provide information during hospital stay for data abstraction, patients who transferred to other hospitals cannot be followed up. Therefore, we used in-hospital mortality as the primary end point. The reference ranges for platelet count, PDW, MPV, and plateletcrit in our laboratory center were 100 to $300 \times 10^3/\mu L$, 9% to 17%, 7.7 to 11.3 fL, and 0.108 to 0.282, respectively.

2.1. Statistical analysis

Normality of data was tested by skewness and kurtosis. Skewness is a measure of the extent to which a probability distribution "leans" to one side of the mean, and kurtosis is a measure of the "peakedness" of the probability distribution. Normally distributed data were expressed as mean ± SD and compared by using *t* test. Otherwise, data were expressed as median and interquartile range and tested using Wilcoxon rank sum test. Variables with a $P < .1$ in univariable analysis were entered into a multivariable logistic regression model to adjust for the odds ratio (OR) of PVIs for mortality. Collinearity was tested using variance inflation factor (VIF) that quantifies the severity of multicollinearity in an ordinary least squares regression analysis. A VIF of 5 or higher indicates a multicollinearity problem [11]. Goodness of fit of the model was tested using Hosmer-Lemeshow tests [12]. Platelet indices were categorized into tertiles of normal range, lower than lower limit, and higher than upper limit. Normal range was used as the reference with an OR of 1. Variables independently associated with mortality were further tested for their association with survival time. Log-rank test was used for the comparison of survival curves between patients with abnormal and normal PVIs. Diagnostic performance of PVIs was investigated using receiver operating characteristic curve. All statistical analyses were performed using the software StataSE 11.0 (College Station, TX). A 2-sided $P < .05$ was considered statistically significant.

3. Results

A total of 139 subjects were excluded according to our predefined exclusion criteria: 30 patients stayed in the ICU for less than 24 hours; 31 patients had missing data on PVIs; 33 patients signed the do-not-resuscitate order; and 45 patients transferred to other hospitals for further treatment, and their follow-up data were unavailable. As a result, a total of 1556 patients were included in the present analysis during the study period (Appendix). There were 1113 survivors and 443 nonsurvivors, with a mortality rate of 28.47%. There were 1021 (65.62%) male patients in the total cohort, and they were more likely to die in-hospital than their female counterparts ($P = .054$). Nonsurvivors were significantly older than survivors (63.1 ± 20.0 vs 60.7 ± 19.0 years, $P = .029$) and had more comorbidity burdens than survivors (median Charlson index: 2 vs 0, $P < .001$). Whereas patients with trauma and cardiovascular diseases were more likely to survive, patients of neurosurgery, post–cardiopulmonary resuscitation, multiorgan failure, and obstetrics/gynecology (OB/Gy) were more likely to die. With respect to laboratory parameters, nonsurvivors had significantly higher PDW (14.4% ± 3.3% vs 13.7% ± 3.0%, $P < .001$), MPV (11.1 ± 1.4 vs 10.5 ± 1.4 fL, $P < .001$), RDW (14.9% ± 2.1% vs 14.2% ± 1.9%; $P < .001$), and WBC (14.9 ± 40.9 vs 11.0 ± 5.8 103/μL, $P = .0024$) than survivors. In contrast, the platelet count ($145.3 \pm 98.6 \times 10^3/\mu L$

Table 2
Mortality OR adjusted for confounding factors

Variables	OR	95% CI	*P* for OR	*P* for Hosmer-Lemeshow goodness of fit	VIF
PDW (%)					
Reference (9-17)	1			.443	
<9	0.65	0.31-1.33	.234		1.05
>17	1.92	1.40-2.65	<.001		1.19
Platelet count ($\times 10^3/\mu L$)					
Reference (100-300)	1			.664	
<100	0.63	0.25-1.62	.341		1.05
>300	0.35	0.22-0.54	<.001		1.27
MPV (fL)					
Reference (7.7-11.3)	1			.489	
<7.7	0.22	0.01-3.48	.280		1.02
>11.3	1.84	1.43-2.37	<.001		1.49
Plateletcrit					
Reference (0.108-0.282)				.522	
<0.108	2.22	1.64-3.02	<.001		1.37
>0.282	0.36	0.24-0.54	<.001		1.29

Odds ratios were adjusted for variables including sex, age, albumin, Charlson index, RDW, WBC, reasons for ICU admission (primary diagnosis), blood transfusion, and hemoglobin. Charlson index was included as a continuous variable.