Journal of Diabetes and Its Complications 30 (2016) 1097–1102

Contents lists available at ScienceDirect

Journal of Diabetes and Its Complications

journal homepage: WWW.JDCJOURNAL.COM

Mean platelet volume-to-lymphocyte ratio: a novel marker of poor short- and long-term prognosis in patients with diabetes mellitus and acute myocardial infarction

Bartosz Hudzik *, Janusz Szkodziński, Andrzej Lekston, Marek Gierlotka, Lech Poloński, Mariusz Gąsior

Third Department of Cardiology, Silesian Center for Heart Disease, SMDZ in Zabrze, Medical University of Silesia in Katowice

ARTICLE INFO

Article history:
Received 28 March 2016
Received in revised form 11 April 2016
Accepted 12 April 2016
Available online 29 April 2016

Keywords:
Mean platelet volume (MPV)
Lymphocyte
Mean platelet volume-to-lymphocyte ratio (MPVLR)
STEMI
Outcomes
Prognosis

ABSTRACT

Introduction: Platelet activation and hyperreactivity plays a pivotal role in developing intravascular thrombus in ST elevation myocardial infarction (STEMI). Mean platelet volume (MPV), which is readily available in clinical settings, has been linked to poor prognosis following STEMI. Recently, platelet-to-lymphocyte ratio (PLR) has emerged as a new marker of worse outcomes linking inflammation and thrombosis. We investigated the prognostic significance of the new marker, MPVLR, in diabetic patients with STEMI undergoing percutaneous coronary intervention (PCI).

Methods: A total of 623 patients with diabetes mellitus and STEMI undergoing primary PCI were enrolled and divided based on the median MPVLR on admission into two groups: group 1 (N = 266) with an MPVLR ≤4.46 and group 2 (N = 257) with an MPVLR >4,46.

Results: Despite similar clinical features patients with elevated MPVLR (group 2) had worse angiographic characteristic suggestive of a higher thrombus burden. In-hospital and one-year mortality was higher in group 2. ROC analysis revealed moderate diagnostic value in predicting in-hospital mortality (adjusted HR 1.13; 95% CI 1.04–1.23; P = 0.003; MPVLR cut-off >6.13) similar to that of PLR a good diagnostic value in predicting long-term mortality (adjusted HR 1.52; 95% CI 1.42–1.63; P < 0.0001; MPVLR cut-off >5.88) better than that of PLR. MPVLR remained an independent risk factor of early and late mortality.

Conclusions: To the best of our knowledge, this is the first ever study that has investigated MPVLR. Despite similar clinical characteristics, patients with elevated MPVLR had worse angiographic features which may indicate a greater thrombus burden. Elevated MPVLR is an independent risk factor of early and late mortality following STEMI. In addition, it has similar value to PLR in predicting in-hospital mortality, and a better value than PLR in predicting long-term mortality.

1. Introduction

The role of platelets has been implicated in the formation and progression of atherosclerosis (Nording, Seizer, & Langer, 2015). Moreover, platelets take the center stage in acute coronary syndromes (ACS) when they form a thrombus upon the ruptured atherosclerotic plaque. Platelet activation and hyperreactivity plays a pivotal role in developing intravascular thrombus (May et al., 2007). In recent years, there has been an increasing number of reports linking diabetes mellitus (DM) to platelet dysfunction (Vinik, Erbas, Park, Nolan, & Pittenger, 2001). Platelets of diabetic patients are characterized by dysregulation of several signaling pathways, which leads to increased platelet reactivity. This may play a role not only in the higher risk of developing ST-elevation myocardial infarction (STEMI) and the worse outcomes observed in DM, but also in the larger proportion of DM patients with inadequate response to antiplatelet agents compared with non-DM patients (Ferreiro & Angiolillo, 2011). Platelet size has been reported to reflect its activity. Larger-size platelets are metabolically and enzymatically more active (Thompson, Eaton, Princiotta, Rushin, & Valeri, 1982). Experimental data support the central role of platelets. However, methods of testing platelet activity may be very time consuming, expensive, and technically difficult (Michelson, 2009). Mean platelet volume (MPV), which is readily available in clinical settings, has been linked to poor prognosis following ST-elevation myocardial infarction (STEMI) (Huczek et al., 2005; Lekston et al., 2014).

Conflict of interests: none.
Funding: none.

* Corresponding author at: Third Department of Cardiology, Silesian Center for Heart Disease, Medical University of Silesia, Curie-Sklodowska 9, 41-800 Zabrze, Poland. Tel.: +48 323733788; fax: +48 322732679.
E-mail address: bartekh@mp.pl (B. Hudzik).

http://dx.doi.org/10.1016/j.jdiacomp.2016.04.010
1056-8727/

Table 1
Patients' baseline and clinical characteristics.

	Group 1, N = 266	Group 2, N = 257	P
Age, years (mean ± SD)	64 ± 9	64 ± 10	0.7
Men, N (%)	112 (42.1%)	105 (40.8%)	0.7
Systemic hypertension, N (%)	177 (74.0%)	181 (70.4%)	0.3
Prior myocardial infarction, N (%)	82 (30.8%)	77 (30.1%)	0.8
Time from symptom onset, hours [median (interquartile range)]	4.5 (3.0–7.5)	5.0 (3.0–7.0)	0.8
Cardiogenic shock, N (%)	31 (11.6%)	38 (14.8%)	0.3
Aspirin, N (%)	260 (97.7%)	170 (97.7%)	0.9
Clopidogrel, N (%)	266 (100%)	257 (100%)	1.0
Insulin*, N (%)	109 (41.0%)	110 (42.8%)	0.7
Metformin*, N (%)	165 (62.0%)	173 (65.0%)	0.3
Sulfonylureas*, N (%)	93 (35.0%)	84 (32.7%)	0.5
LVEF, (%) [median (interquartile range)]	42 (35–48)	42 (35–47)	0.2
Hospital stay, days [median (interquartile range)]	9 (7–12)	8 (6–11)	0.03
In-hospital death, N (%)	24 (9.0%)	46 (17.9%)	0.03

SD, standard deviation; LVEF, left ventricular ejection fraction.
* Given the effect of hypoglycemic therapy on platelet function (Papazafiropoulou, Papanas, Pappas, Maltezos, & Mikhailidis, 2015) we reported the use of hypoglycemic agents on admission; some patients were on more than one hypoglycemic agent.

Table 3
Laboratory findings.

	Group 1, N = 266	Group 2, N = 257	P
Leukocytes (10^3/mm^3)	13.8 ± 5.3	14.4 ± 5.5	0.5
Lymphocytes (10^3/mm^3)	2.4 ± 0.2	1.9 ± 0.5	<0.0001
Erythrocytes (10^6/mm^3)	4.6 ± 0.6	4.5 ± 0.6	0.4
Haemoglobin (mmol/L)	8.7 ± 1.5	8.7 ± 1.6	0.9
Hematocrit (%)	42 ± 5	41 ± 5	0.8
Platelet count (10^3/mm^3)	229 ± 71	211 ± 62	0.2
Mean platelet volume (fL)	8.4 (7.9–10.0)	11.0 (10.1–12.9)	<0.0001
Platelet distribution width (fL)	9.3 (8.1–10.1)	10.0 (8.9–10.9)	<0.0001
Platelet-to-lymphocyte ratio	98 (78–118)	120 (88–166)	<0.0001
Mean platelet volume-to-lymphocyte ratio	3.64 (3.36–4.00)	5.67 (4.94–8.20)	<0.0001
Admission glycemia (mmol/L)	8.9 ± 3.9	9.1 ± 4.0	0.4
Total cholesterol (mmol/L)	5.7 (5.0–6.7)	5.8 (4.9–6.6)	0.8
HDL cholesterol (mmol/L)	1.3 (1.1–1.7)	1.3 (1.1–1.5)	0.8
LDL cholesterol (mmol/L)	3.6 (2.9–4.4)	4.1 (3.2–4.6)	0.09
Triglycerides (mmol/L)	1.4 (0.8–2.1)	1.1 (0.8–1.8)	0.1
Serum creatinine (μmol/L)	84 (72–100)	84 (70–99)	0.9
eGFR (mL/min per 1.73 m^2)	67 (58–88)	72 (60–85)	0.6

Inflammatory process arising from the effects of hyperglycemia, insulin resistance, and modified free fatty acid metabolism predisposes diabetic patients to endothelial dysfunction, thrombogenesis, monocyte activation, and altered smooth muscle cell migration (Armstrong, Rutledge, & Rogers, 2013). All of which converge to create an increased atherosclerotic plaque burden. Inflammatory process has also been linked to an increased risk of MI and poor prognosis. Numerous studies have shown that of IL-6 and C-reactive protein (CRP) concentrations correlate with infarct size, reperfusion, short-term and long-term prognosis (Frangogiannis, Smith, & Entman, 2002; Ziakas et al., 2006). Recently, platelet-to-lymphocyte ratio (PLR) has emerged as a new and strong marker of worse outcomes in acute coronary syndromes (Azab, Shah, Akerman, & McGinn, 2012; Hudzik et al., 2015; Kurtul et al., 2014). However, it was first introduced as an inflammatory marker that predicted poor outcomes in cancer patients (Smith et al., 2009).

Pathophysiology-wise, platelet activity, rather than platelet count itself, plays an essential role in acute coronary syndromes. In comparison to other studies, we decided to use the information on platelet activity based on MPV and the interaction between platelets and inflammatory system based on PLR to form a new MPV-to-lymphocyte ratio (MPVLR). We set out to study the prognostic significance of the new marker, MPVLR, in diabetic patients with ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI). In view of the fact that platelet size features platelet activity more accurately than platelet count itself, the notion of replacing platelet count in the PLR for MPV to form MPVLR seems plausible.

Table 2
Angiographic findings.

	Group 1, N = 266	Group 2, N = 257	P
Infarct-related artery			
• LAD, N (%)	105 (39.5%)	111 (43.2%)	0.8
• Cx, N (%)	42 (15.8%)	36 (14.0%)	
• RCA, N (%)	112 (42.1%)	103 (40.1%)	
• Other, N (%)	7 (2.6%)	7 (2.7%)	
Multivessel CAD, N (%)	138 (51.9%)	129 (50.2%)	0.6
Initial TIMI flow, N (%)			
• 0	148 (55.6%)	166 (64.8%)	0.04
• 1	44 (16.5%)	44 (17.2%)	
• 2	51 (19.2%)	38 (14.5%)	
• 3	23 (8.7%)	9 (3.5%)	
Final TIMI flow, N (%)			
• 0	12 (4.5%)	22 (8.6%)	0.03
• 1	3 (1.1%)	3 (1.2%)	
• 2	12 (4.5%)	28 (10.6%)	
• 3	239 (89.9%)	204 (79.6%)	

2. Material and methods

The study conforms to the Declaration of Helsinki. Informed consent for data analysis was obtained from the patients according to the Polish law on patients' rights regarding data registration. Approval for analyzing recorded data was waived by the local bioethics committee on human research given the retrospective nature of the study.

Patients admitted with diagnosis of STEMI, within 12 h from symptom onset were enrolled in the study. Exclusion criteria have been described previously (Hudzik et al., 2015).

A total of 523 patients with diabetes mellitus and STEMI undergoing primary PCI were enrolled. Based on the median of admission MPVLR the study population was divided into two groups: group 1 (N = 266) with an MPVLR ≤4.46 and group 2 (N = 257) with an MPVLR >4,46. MPVLR was calculated as MPV divided by lymphocyte count (10^3/mm^3).

All patients received loading doses of antiplatelet medications (aspirin, clopidogrel) before admission to our hospital (either in the referring hospital or ambulance) according to the guidelines.

Detailed information on venous blood collection and handling has been described in detail previously (Hudzik et al., 2015). Diabetes mellitus was defined as: (a) pre-existing condition diagnosed before STEMI (patients on insulin, oral glucose-lowering drugs or on a diet), (b) newly diagnosed diabetes mellitus based on fasting plasma glucose (FPG) ≥7.0 mmol/L or 2-h plasma glucose ≥11.1 mmol/L during an oral glucose tolerance test (OGTT) (Ryden et al., 2007). To avoid acute hyperglycaemia, FPG was taken into consideration after the third day of hospital stay. For that reason, OGTT was performed on day four of hospital stay or later. STEMI was defined as: 1) ST-segment elevation consistent with MI of at least 2 mm in at least two contiguous precordial leads and/or ST-segment elevation of at least 1 mm in two or more limb leads or new left bundle branch block, and 2) positive cardiac necrosis markers (CK-MB and/or troponin). Patients received 300 mg of acetylsalicylic acid (ASA) loading dose and 600 mg of clopidogrel loading dose, followed by 75 mg of ASA maintenance dose and 75 mg of clopidogrel maintenance dose (Silber et al., 2005). Coronary angiography and percutaneous coronary interventions were performed using standard protocols and guidelines. A culprit lesion was described in the presence of an acute occlusion, intraluminal filling