Utilization of Mean Platelet Volume (MPV) to Predict Perfusion Defects in Myocardial SPECT in Diabetic and Non-Diabetic Patients

Maryam Arefnia
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

Toktam Hosseinnezhad Ariani
Mashhad University of Medical Sciences

Mohammadali Ghodsirad (ghodsiradma@sbmu.ac.ir)
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

Toktam alirezaei
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

Elinaz Hosseinzade
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

Mahasti Amoui
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

Elahe pirayesh
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

Ghazal Norouzi
Clinical research development unit of Shohada Tajrish hospital Shahid Beheshti University of medical sciences

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Research Article

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Abstract

Introduction

; An increase in the average volume of platelets has been associated with poor outcomes in patients with acute coronary syndrome. The aim of this study was to assess the use of myocardial perfusion scans to study the association between MPV and myocardial perfusion abnormalities in patients with and without diabetes mellitus (DM). diabetic and non-diabetic patients.

Materials and Methods

; This was a cross-sectional study. Forty-nine patients with known type 2 diabetes DM and without obvious cardiovascular symptoms and 49 healthy individuals were included. A myocardial perfusion scan was performed in rest and stress with dipyridamole/dobutamine/exercise testing. Data entered SPSS software and analyzed. A *p* value below 0.05 was considered as statistically significant.

Results;

In total, 98 participants including 49 patients with DM and 49 healthy individuals were included. Laboratory variables as well as cardiac scan items including Summed Stress Score (SSS), Summed Rest Score (SRS), Summed Difference Score (SDS), Ejection Fraction (EF) and End Systolic Volume (ESV) were not statistically different in the two groups. Only the average platelet count was higher in controls than diabetics. In regression analysis, by one-unit increase in MPV, the SRS increased by an average of 0.46 (CI; 0.08–0.83 β: 0.46), only in healthy controls.

Discussion and Conclusion

; MPV is a predictor of myocardial perfusion defects, which could be measured easily for patients in different clinical scenarios as a herald for coronary artery disease, especially in healthy individuals.

Background

Platelets play a central role in the pathophysiology of coronary heart disease. An increase in the average volume of platelets has been associated with poor outcomes in patients with acute coronary syndrome [1–3]. Various researches have shown an association between MPV and CAD (Coronary Artery Disease) severity. Moreover, it has been proposed that MPV could be a useful marker in patients with CAD to assess the severity of coronary atherosclerosis [4, 5]. An independent association has been found between high MPV and myocardial perfusion defects. In addition to CAD, the average platelet count is related to other cardiovascular events [5, 6]. Moreover, MPV can be easily measured. On the other hand, MPV has been associated with increased plasma glucose levels and can be a cost-effective way to

monitor type 2 Diabetes Mellitus (DM). DM itself leads to many complications such as cardiovascular diseases [7, 8].

Most patients with DM (about two-thirds) die from cardiac diseases, stroke, or peripheral vascular diseases. The prevalence of coronary artery disease in diabetic patients is high, and ischemia and myocardial infarction in these patients are often without clear clinical manifestations [9–12]. Diagnosis of coronary artery disease in patients with DM is essential for early treatment.

Myocardial perfusion scan is a fully approved and standardized for examining myocardial function. The diagnostic value of this scan has been confirmed in many situations, including in patients with DM or those undergoing cardiac surgery (surgery or PCI) [13, 14]. If the myocardial perfusion scan result is abnormal and the ischemia is moderate to high, the mortality rate would be high if an effective intervention is not performed promptly. Myocardial perfusion scan has a high sensitivity and specificity of about 90%. The prognostic value of cardiac scanning has also been studied in many studies. For example, one study found that patients with X syndrome would have worse prognosis if the myocardial scan is abnormal [15–17].

Invasive treatment and revascularization improves the patient's prognosis in case of moderate and severe ischemia, and in mild cases of ischemia, patients would benefit more from medical treatment [18, 19].

Platelet volume is a marker of their activity and is measured in the form of mean platelet aggregation (MPV). MPV has recently been used as a new prognostic factor in coronary heart disease [20]. Therefore, the aim of this study was to assess the use of myocardial perfusion scans to study the association between MPV and myocardial ischemic severity in patients with DM and healthy individuals. Discriminative aspects of our study compared to similar investigations [21–23] are as follows; first, we extensively assessed different systolic and diastolic indices to find even subtle evidence of CAD in patients with DM, second, we used both the Cedars-Sinai tools Quantitative Perfusion SPECT (QPS) and the Quantitative gated SPECT (QGS) as well as corridor 4DM software (University of Michigan/ Mirada Medical) for better interpretation of scans.

Methods

This was a cross-sectional study. An ethical approval was obtained from the ethics committee of Shahid Beheshti University of Medical Sciences (code IR.SBMU.RETECH.REC.1397.1035). All patients were briefed about the study aims and a written informed consent was also obtained from all participants.

Patient selection: Forty-nine patients with known type 2 DM and without obvious cardiovascular symptoms and 49 healthy controls who were visited in our cardiovascular clinic entered the study. These asymptomatic patients became candidates for stress/rest myocardial perfusion study for either screening purposes or pre-operation evaluation.

Inclusion criteria were age between 35 and 65 years and systolic function above 50% based on recent echocardiography obtained in less than one month. Exclusion criteria were a history of valvular heart disease, ischemic heart disease, abnormal renal or hepatic failure and history of myocardial infarction. Patients with known hematologic disorders were also excluded. The sample size was calculated based on similar studies [24]. Risk factors were assessed and recorded using special research-made questionnaire. A complete blood count and MPV results were obtained using Sysmex - KX-21 system.

Image acquisition: Myocardial perfusion scan was performed in two stages of rest and stress with dipyridamole/dobutamine/exercise testing. The gamma camera used was the Evo-Voxel Siemens with Variable Angle Dual Heads and using the E. soft software (Siemens Medical solutions). Imaging characteristics were Matrix: 64×64, Orbit: 180°, 32 frame from RAO till LPO, 15% window centered on 140-KeV photopeak, Gated: 8 frame per cardiac cycle: acceptance window: 20% and Reconstruction with 3D flash algorithm.

Image interpretation

Images were first reconstructed with 3D flash algorithm using Siemens Syngo® MI Apps (E.soft) and were analyzed and scored visually. Then reconstructed images were checked in QPS, QGS and 4DM software. In case of any inconsistency, MPIs were rechecked to achieve agreement and if any discrepancy remained between visual assessment and results of mentioned software, another qualified nuclear medicine specialist (blind to initial judgment and software results) was asked to evaluate the scan. Scoring of the left ventricular myocardial perfusion during rest and stress was performed using 17 segments model. Normal perfusion is indicated on the scale as zero. While mild and moderate perfusion impairment indicated by 1 and 2, respectively. A score of 3 implies substantial perfusion defect, while a score of 4 is used to show absent perfusion. The Summed Stress Score (SSS) and the Summed Rest Score (SRS) were calculated as a sum of the individual scores from the 17 segments of the polar map obtained during stress and rest and then Summed Difference Score (SDS) was calculated by subtracting the SRS from the SSS (SDS = SSS – SRS) [25].

To assess systolic and diastolic function, as more parameters were available in QGS software, indices from QGS were only recorded and analyzed.

Statistical Analysis

Data entered SPSS software (SPSS Inc. Chicago, Il, The USA) and analyzed. Descriptive variables were reported using mean ± SD. Correlation coefficient was also used to assess the effect of confounding variables. A linear regression was also used to assess the correlation of ischemia risk factors with SSS, SRS and SDS.

Results

In total, 98 participants including 49 patients with DM and 49 healthy individuals were included. The mean age of patients with DM was 61.69 ± 7.32 years. Also, the mean age of healthy individuals was 61.45 ± 6.81 years. In total, 64.3% (63 people) were women (59.2% women in patients with DM and 69.4% of controls). Table I shows the demographic characteristics of participants.

Table I. Comparison of Different Variables in the Study Participants

Variable	Patients with DM (N = 49)	Healthy controls (N = 49)	All (N = 98)	*p* value*
Age (year), Mean ± SD	61.7 ± 69.32	61.6 ± 2.33	61.44 ± 6.81	0.72
Platelet Count (PLT), Mean ± SD	252.65 ± 51.47	281.77 ± 48.24	72 ± 267.7	0.04
Lymphocyte Count *(Lymph)*, Mean ± SD	38.14 ± 91.86	36.15 ± 59.92	37.75 ± 15 ± 0.36	0.45
Neutrophils Count (Neut), Mean ± SD	58.15 ± 24.63	60.16 ± 75.76	59.16 ± 5.17	0.44
White Blood Cell Count (WBC), Mean ± SD	8.1 ± 21.91	7.1 ± 99.73	8.1 ± 1.82	0.56
	Median (IQR)	Median (IQR)	Median (IQR)	p value**
Summed Stress Score (SSS)	2 (4)	2 (7)	2 (5)	0.51
Summed Rest Score (SRS)	0 (1)	0 (2)	5 (1)	0.89
Summed Differences Score (SDS)	1 (3)	1 (3)	1 (3)	0.7
Ejection Fraction (EF)	70 (7)	65 (15.5)	65 (13)	0.05
End-Systolic Volume (ESV)	19 (11)	16 (10)	17.5 (12)	0.26
End-Diastolic Volume (EDV)	50 (26)	55 (17)	54 (22)	0.78
Mean Platelet Volume (MPV) (fl)	9.65 (2.35)	10 (2.3)	9.9 (2.3)	0.56
PLT to Neut Ratio	4.33 (2.18)	4.59 (2.64)	4.44 (2.71)	0.45
Neut to Lymph Ratio (NLR)	1.45 (1.26)	1.57 (1.39)	1.5 (1.33)	0.33
*Using T Test, ** using Mann Whitney Test				

According to Table I, healthy individuals had significantly higher ischemia in LCX territory ($p = 0.03$). There was no difference between the two groups regarding other artery domains.

Based on Mann-Whitney test, laboratory variables as well as cardiac scan items including SSS, SRS, SDS, EF, ESV were not statistically different between the two groups. Only the average PLT count was higher in healthy individuals than those with DM. There was no meaningful difference regarding MPV between the two groups.

According to linear regression, only the correlation between SRS and MPV (r = 0.32 r = 0.28 for SRS) in healthy subjects was significant. As with increased MPV, the probability of an abnormal scanning was increased ($P < 0.05$). Figures 1 and Table 2 show the correlation between SRS, SSS and SDS with MPV in the two groups.

The correlation between ischemia variables and laboratory indices of MPV, Plt/Neut and Neut/Lymph was checked using linear regression in the two groups. Only the correlation between SRS and MPV in healthy individuals was statistically significant and the others were not significant ($p > 0.05$). By each unit increase in MPV, the SRS increased by an average of 0.46 (CI; 0.08–0.83 β: 0.46) (Table 2).

Table 2
Linear Regression between Ischemia Variables and Laboratory Findings in the Two Groups

Variables		SSS	*p* value	SRS	*p* value	SDS	*p* value
Patients with DM	MPV	0.45	0.22	0.38	0.14	0.06	0.85
	Plt/Neut	-0.4	0.2	-0.27	0.2	-0.16	0.57
	Neut/Lymph	-0.14	0.7	-0.25	0.32	0.08	0.79
Healthy Controls	MPV	0.58	0.08	0.46	0.01	0.12	0.59
	Plt/Neut	-0.09	0.74	0.11	0.47	-0.2	0.29
	Neut/Lymph	0.08	0.81	0.23	0.23	-0.15	0.52
SRS: Summed difference Score, SRS: Summed Rest Score, MPV: Mean Platelet Volume,							

Plt: Platelet, Neut: Neutrophil, Lymph: Lymphocyte

Discussion

Previous studies have shown that patients with a higher MPV have a greater risk of death due to IHD (Ischemic Heart Disease), with hazard ratios similar to those reported for obesity or smoking [26]. In our study there was no meaningful association between myocardial perfusion defect and mean platelet volume in patients with DM, however, there was a statistically meaningful association in healthy participants. As shown, by one-unit increase of MPV, the SRS increased by an average of 0.46, which means higher MPV values may be an indicator of previous infarctions but not ischemia in healthy population. The association between increased MPV and myocardial infarction was previously reported by other investigators as well [27, 28], but was confirmed only in healthy individuals in our study.

This is in contrast to Savas Sarikaya et al. investigation. They found a statistically significant difference between MPV and myocardial perfusion defect in patients with DM as well. They claimed that higher MPV in patients with DM was associated with myocardial perfusion defects, which could be considered as an indicator of ischemia [29]. The difference might be due to different designs as they did not include patients without DM in their study. Also, some other confounding variables might have an effect like differences in sample size and ischemia variables. However, our patients with DM were asymptomatic, which might need more time to develop complications.

Vascular complications including macrovascular (CAD, peripheral vascular disease and stroke) and microvascular (neuropathy, retinopathy and nephropathy) ones are common in DM. High blood sugar damages vascular endothelium leading to the above problems. Therefore, DM has been considered as an independent risk factor for atherosclerotic cardiovascular disorders [30–32], as CVD is considered the leading underlying reason for mortality in DM patients [33]. On the other hand, DM causes asymptomatic CAD in some patients.

Cardiac perfusion scans have been widely used to predict coronary diseases. It might show perfusion abnormalities despite a normal coronary angiogram, which is probably due to microangiopathy and endothelial dysfunction and following subtle decreased tissue oxygenation [34].

Mean Platelet Volume is indicative of platelet function. It is believed that platelets with denser granules are more active in some processes such as inflammation, coagulation, thrombosis and atherosclerosis. This might lead to higher probability of coronary thrombosis and ischemia. Platelets with higher MPV contain more procoagulant membrane proteins, serotonin, beta-thromboglobulin and prothrombogenic thromboxane A2 [35–38].

In another investigation, MPV was found to be higher in patients with cardiac syndrome X and coronary artery disease compared to controls. They indicated that it verifies the role of higher MPV in subclinical atherosclerosis [39].

Despite the fact, many studies have shown higher MPV levels in patients with DM. Kodiatte et al. showed that significantly higher MPV levels in patients with DM compared to healthy individuals. They also indicated a strong correlation between MPV with fasting blood glucose, postprandial glucose and HbA1C levels [40]. Semi Ozturk also found higher levels of MPV in patients with ischemic cardiomyopathy. They claimed that patients with non-viable myocardium had significantly higher levels of MPV. They recommended to consider MPV as a cheap, practical and easily measurable index which could be used in the prognosis of ischemic cardiomyopathy [41].

Papanas et al. assessed MPV level in a quite large number of patients. They compared MPV in 416 patients with type 2 DM and healthy individuals. They also evaluated the association between MPV and diabetic complications. They finally reported that MPV is higher in patients with type 2 DM compared to healthy ones. Despite the fact, MPV was more increased in patients with microvascular complications such as retinopathy or micro-albuminuria [42].

The reason why we did not find a statistically significant difference between myocardial perfusion defect and mean platelet volume in patients with DM is challenging. However, such an association in healthy controls could be due to small number of participants or a selection bias as a consecutive sampling method might not be enough precise. Moreover, our patients with DM were asymptomatic which might need more time to develop microvascular complications. There is no doubt that mean platelet volume can be measured as part of routine assessment in patients with cardiovascular disorders.

We had some limitations. First our sample size was quite small, which might be responsible for a non-significant difference in patients with DM. This could be addressed in further investigations as well. Despite the fact, the novelty of our study was its grouping and study design. We could not find any similar study to compare MPV in patients with and without DM who underwent myocardial perfusion scan.

Conclusion

MPV is a predictor of myocardial perfusion defects, which could be measured easily for patients in preoperative management as a herald for subclinical coronary atherosclerosis, especially in non-diabetics.

List Of Abbreviations

MPV
Mean platelet volume
DM
Diabetes Mellitus
CAD
Coronary Artery Disease
SSS
Summed Stress Score,
SRS
Summed Rest Score
SDS
Summed Difference Score
EF
Ejection Fraction
ESV
End Systolic Volume

Declarations

Ethics approval and consent to participate: This was a cross-sectional study. An ethical approval was obtained from the ethics committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1397.1035).

All patients were briefed about the study aims and a written consent was also obtained from all participants.

All procedures were done according to the EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision.

Consent for publication: All authors agreed for publication.

Availability of data and material: *The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.*

Competing interests: No competing interest

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Conflict of interests : None

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Figures

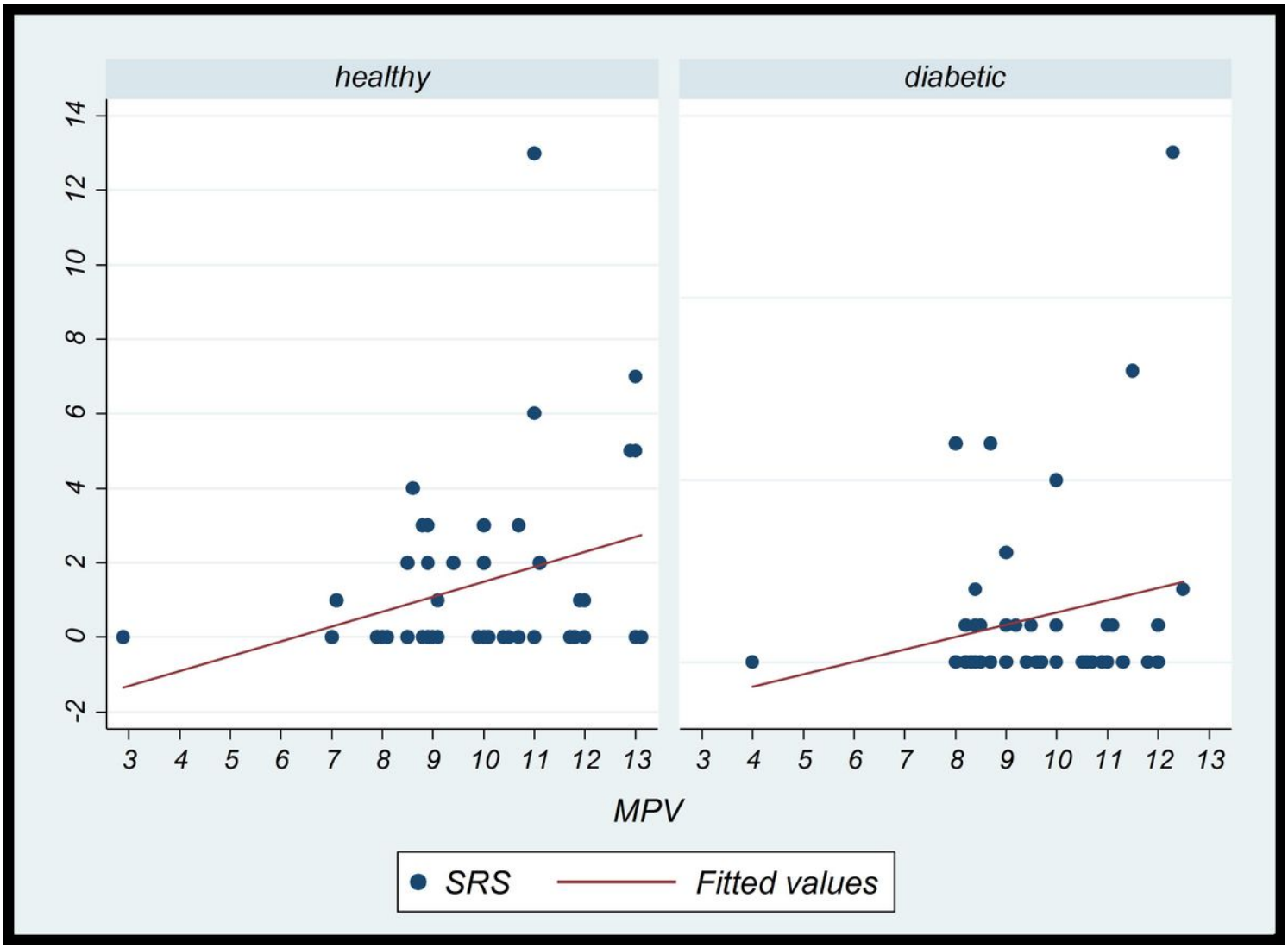

Figure 1

The Correlation between SRS and Mean Platelet Volume in the Two Groups