Original Article

Utilization of Mean Platelet Volume for Predicting Ischemic Heart Disease in Diabetic and Non-Diabetic Patients

Maryam Arefnia[1,2], Toktam Hosseinnezhad Ariani[4], Mohammadali Ghodsirad[1,2*], Toktam Alirezaei[1,3], Elinaz Hosseinzadeh [1,2], Mahesti Amoui[2], Elaheh Pirayesh[2], Ghazaal Norouzi[2]

[1]Clinical research development unit of Shohada Tajrish Hospital Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Nuclear medicine department, Shohada Tajrish hospital, School of medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Cardiology department of Shohada Tajrish hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran

Received: 20 October, 2024; Accepted: 27 October, 2024

DOI: 10.22037/nbm.v13i1.46513

Abstract

Background: This study aimed to evaluate the relationship between mean platelet volume (MPV) and myocardial perfusion abnormalities in patients with and without Type 2 diabetes mellitus (DM) using myocardial perfusion scans.

Materials and Methods: This cross-sectional study compared 49 patients with Type 2 DM without overt cardiovascular symptoms with 49 healthy controls. Both groups underwent myocardial perfusion scans at rest and under stress conditions. Risk factors were assessed and recorded using a special research-made questionnaire. A complete blood count and MPV results were obtained using the Sysmex - KX-21 system. Data were analyzed using SPSS, with a p-value below 0.05 considered statistically significant.

Results: No significant differences were observed between the two groups in terms of Summed Stress Score (SSS), Summed Rest Score (SRS), Summed Difference Score (SDS), Ejection Fraction (EF), and End Systolic Volume (ESV). The only marked variance was a higher average platelet count in the control group. Regression analysis revealed that a one-unit increase in MPV correlated with a 0.46 average increase in SRS in the control group (CI: 0.08-0.83, β: 0.46).

Conclusion: MPV may serve as a predictive marker for myocardial perfusion abnormalities, especially in individuals without diabetes. This simple metric could act as an early indicator for coronary artery disease.

Keywords: Mean platelet volume, Myocardial perfusion scan, Diabetes mellitus, Coronary heart disease

***Corresponding Author:** Dr. Mohammadali Ghodsirad, Nuclear medicine specialist, Assistant professor of nuclear medicine, Shohada Tajrish Hospital, Shahid Beheshti university of medical science. Fellow of the Asian Nuclear Medicine Board (FANMB), FELLOW of European Board of Nuclear Medicine (FEBNM). Email: gho.rad81@gmail.com

Please cite this article as: Arefnia M, Hosseinnezhad Ariani.T, Ghodsirad.MA, Alirezaei.T, Hosseinzadeh E, Amoui. M, et al. Utilization of Mean Platelet Volume for Predicting Ischemic Heart Disease in Diabetic and Non-Diabetic Patients. Novel Biomed. 2025;13(1):39-45.

Introduction

Platelets play a pivotal 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], and various types of research have shown an association between mean platelet volume (MPV) and coronary artery disease (CAD)[4,5]. Moreover, it has been proposed that MPV could be a useful marker in patients with CAD to assess the severity of coronary

atherosclerosis[6,7]. An independent association has been found between high MPV and myocardial perfusion defects. Large platelets also increase plasma glucose levels in diabetes mellitus (DM). DM leads to many complications, such as cardiovascular diseases[8,9]; thus, measuring MPV hypothetically can be a cost-effective way to monitor type 2 DM and its cardiovascular complications.

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[10-13], so the diagnosis of coronary artery disease in patients with DM is essential for early treatment. Invasive treatment and revascularization improve the patient's prognosis in cases of moderate and severe ischemia, and in mild cases of ischemia, patients would benefit more from medical treatment[14,15].

A myocardial perfusion scan is a fully approved and standardized method for examining myocardial vascularity and 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)[16,17]. 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 latest related metanalysis confirmed the relation between larger MPV and coronary artery disease[18] but issues like the difference between diabetics and non-diabetics were not addressed, furthermore, there is still some inconsistency and uncertainty about the role of MPV as a screening tool for CAD[4,5,18-22]; therefore, this study aimed to assess whether MPV can predict perfusion abnormalities in diabetic and non-diabetics, using gated myocardial perfusion scintigraphy. Discriminative aspects of our study compared to similar investigations[23-25] 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 study was a cross-sectional study. Ethical approval was obtained from the ethics committee of Shahid Beheshti University of Medical Sciences. All patients were briefed about the study aims, and ten informed consents were also obtained.

Patient selection: Forty-nine patients with known type 2 DM without obvious cardiovascular symptoms and 49 healthy controls who visited 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 a history of myocardial infarction. Patients with known hematologic disorders were also excluded. The sample size was calculated based on similar studies[26]. Risk factors were assessed and recorded using a special research-made questionnaire. A complete blood count and MPV results were obtained using the Sysmex - KX-21 system.

Image acquisition: Myocardial perfusion scan was performed in two stages of rest and stress (two-day protocol) with dipyridamole/dobutamine/exercise testing. The gamma camera used the Symbia Evo Excel with Variable Angle Dual Heads and the E. soft software (Siemens Medical Solutions). Imaging characteristics were Matrix: 64×64, Orbit: 180°, 32 frames from RAO till LPO, 15% window centered on 140-KeV photopeak, Gated: 8 frames per cardiac cycle: acceptance window: 20% and Reconstruction with 3D flash algorithm. (4 iterations, 4 subsets) No attenuation correction was applied.

Image interpretation: Images were first reconstructed with a 3D flash algorithm using Siemens Syngo® MI Apps (E.soft). In line with EANAM guidelines of myocardial perfusion Scintigraphy[27], all scans were first checked visually, and SSS, SRS, and SDS were calculated based on visual assessment. Results were

checked in 4DM, QPS, and QGS. In case of any inconsistency between visual inspection and software (different interpretation in different myocardial walls and segments, not subtle difference in scoring), MPIs were rechecked to achieve agreement and if any discrepancy remained between the visual assessment and results of the 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 a 17-segment model. Normal perfusion is indicated on the scale as zero. While mild and moderate perfusion impairments were 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 the Summed Difference Score (SDS) was calculated by subtracting the SRS from the SSS (SDS = SSS – SRS)[28].

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 were entered into SPSS software (SPSS Inc. Chicago, Il, The USA) and analyzed. Descriptive variables were reported using mean ± SD. The correlation coefficient was also used to assess the effect of confounding variables. We used Shapiro Wilk test to assess the normal distribution of data and parameters with normal distribution were compared with the T test and those without normal distribution were compared with Mann Whitney Test. A linear regression was also used to assess the correlation of ischemia risk factors with SSS, SRS, and SDS.

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

Results

A total of 98 participants in patients with DM and 49 healthy individuals were included. The mean age of patients with DM was 61.69 ± 7.32 years. Also, the

Table 1. 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, Mean ± SD	252.65 ± 51.47	281.77 ± 48.24	72 ± 267.7	0.04
Lymphocyte count, Mean ± SD	38.14 ± 91.86	36.15 ± 59.92	37.75 ± 15 ± 0.36	0.45
Neutrophils count, Mean ± SD	58.15 ± 24.63	60.16 ± 75.76	59.16 ± 5.17	0.44
White blood cell count, Mean ± SD	8.1 ± 21.91	7.1 ± 99.73	8.1 ± 1.82	0.56
Variable	**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 ml)	19 (11)	16 (10)	17.5 (12)	0.26
End-Diastolic Volume (EDV (ml)	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

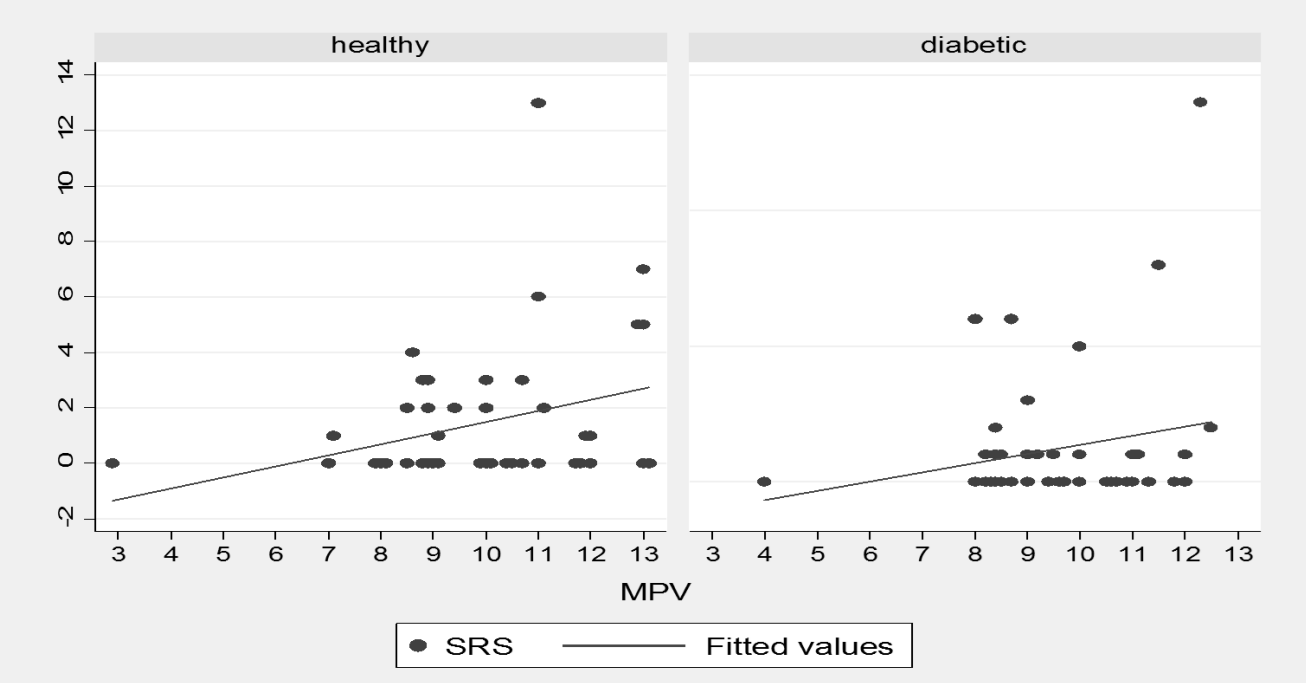

Figure 1. The Correlation between SRS and Mean Platelet Volume in the Two Groups.

mean age of healthy individuals was 61.45 ±6.81 years. In total, 64.3% of participants (63 people) were women (59.2% in DM and 69.4% in control groups, respectively).

No significant difference was noted in the female-to-male ratio in the two groups *(P:0.02)*, with 23 and 25 male patients in diabetic and non/diabetic groups, respectively. Table I shows the demographic characteristics of participants: 10 patients in the non-diabetic group and 6 patients in the diabetic group had abnormal MPI.

Based on the Mann-Whitney test, laboratory variables, and cardiac scan items, including SSS, SRS, SDS, EF, and 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 for SRS) in healthy subjects was significant. As with increased MPV, the probability of an abnormal scanning was increased (*P* <0.05). With each unit increase in MPV, the SRS increased by an average of 0.46 (CI; 0.08-0.83 β: 0.46). Figure 1 shows the correlation between SRS and MPV in the two groups.

The correlation between MPI variables and laboratory indices of Plt/Neut, and Neut/Lymph was also checked using linear regression in the two groups and the result was not statistically significant (*p* >0.05).

Discussion

Mean Platelet Volume is indicative of platelet function. Platelets denser granules are more ac believed to be Platelets with higher MPV and contain more procoagulant membrane proteins, serotonin, β-Thromboglobulin, and prothrombogenic thromboxane A2, and this might lead to a higher probability of coronary thrombosis and ischemia. 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[29].

Many studies have shown higher MPV levels in patients with DM. Kodiatte et al. showed significantly higher MPV levels in patients with DM than in healthy individuals. They also indicated a strong correlation between MPV and fasting blood glucose, postprandial glucose, and HbA1C levels[30]. 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 considering MPV as a cheap, practical, and easily measurable index that could be used to predict ischemic cardiomyopathy[31]. Papanas et al. assessed MPV levels 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 (in line with many other studies) reported that MPV is higher in patients with type 2 DM than healthy ones. MPV was increased in patients with microvascular complications like micro-albuminuria[21,32-35]. Larger MPV has also been associated with high morbidity and poor prognosis in many conditions like retinopathy[36,37] and other vascular diseases[38] in diabetics as well as stroke[39] and inflammatory diseases in the general population[40].

It should be remembered that vascular complications, including macrovascular (CAD, peripheral vascular disease, and stroke) and microvascular (neuropathy, retinopathy, and nephropathy) are common in DM. High blood sugar damages vascular endothelium, leading to the above problems. Therefore, DM has been considered an independent risk factor for atherosclerotic cardiovascular disorders[41-43], and CVD is considered the leading underlying reason for mortality in DM patients[44]. DM causes asymptomatic CAD in some patients, and Cardiac perfusion scans have been widely used to diagnose and screen coronary diseases. It might show perfusion abnormalities despite a normal coronary angiogram, probably due to microangiopathy and endothelial dysfunction and following subtle decreased tissue oxygenation[45].

Previous studies have shown that patients with a higher MPV have a greater risk of death due to CAD, with hazard ratios similar to those reported for obesity or smoking[46]. In our study, there was no meaningful association between myocardial perfusion defects and mean platelet volume in patients with DM; however, there was a statistically meaningful association between healthy participants. As shown by a one-unit increase of MPV, the SRS increased by an average of 0.46, which means higher MPV values may indicate previous infarctions but not ischemia in the non-diabetic population. The association between increased MPV and myocardial infarction was previously reported by other investigators as well[47,48] but was confirmed only in healthy individuals in our study. This contrasts with Sarikaya et al. investigation. They found a statistically significant difference between MPV and myocardial perfusion defect in patients with DM. They claimed that higher MPV in patients with DM was associated with myocardial perfusion defects[49]. This difference may be partly due to confounding factors not considered in the Sarikaya study.

The reason we did not find a statistically significant difference between myocardial perfusion defects and mean platelet volume in patients with DM is challenging but was noted in other studies as well[4,50] and may imply inherently larger platelets in diabetics[51], furthermore, our patients with DM were asymptomatic which might need more time to develop microvascular complications. There is no doubt that MPV can be measured as part of routine assessment in patients with cardiovascular disorders[52], but with caution in diabetics.

We had some limitations. First, our sample size was relatively small, which might be responsible for a non-significant difference in patients with DM. This could be addressed in larger studies. Despite this 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.

Conclusion

We believe that MPV is a predictor of myocardial perfusion defects and could be measured easily in a wide variety of patients in different clinical scenarios as a herald for undiagnosed CAD, especially in non-diabetics.

Acknowledgment

None.

Conflict of interest

The authors further declare that they have no conflict of interest.

References

1. Dorsam RT, Kunapuli SP. Central role of the P2Y 12 receptor in platelet activation. J Clin Invest. 2004;113(3):340-5.
2. Kamath S, Blann A, Lip G. Platelet activation: assessment and quantification. European heart journal. 2001;22(17):1561-71.
3. Yilmaz MB, Cihan G, Guray Y, et al. Role of mean platelet volume in triagging acute coronary syndromes. Journal of thrombosis and thrombolysis. 2008;26(1):49-54.
4. De Luca G, Verdoia M, Cassetti E, et al. Mean platelet volume is not associated with platelet reactivity and the extent of coronary artery disease in diabetic patients. Blood Coagulation & Fibrinolysis. 2013;24(6):619-24.
5. Sahin S, Altunkas F, Karaman K, et al. Mean platelet volume is associated with myocardial perfusion defect in diabetic patients : research article. South African Journal of Diabetes and Vascular Disease. 2016;13(2):77-80.
6. De Luca G, Santagostino M, Secco GG, et al. Mean platelet volume and the extent of coronary artery disease: results from a large prospective study. Atherosclerosis. 2009;206(1):292-7.
7. Gurbel PA, Bliden KP, Hayes KM, Tantry U. Platelet activation in myocardial ischemic syndromes. Expert review of cardiovascular therapy. 2004;2(4):535-45.
8. Varon D, Shai E. Platelets and their microparticles as key players in pathophysiological responses. Journal of Thrombosis and Haemostasis. 2015;13:40-6.
9. Storey RF. The P2Y 12 receptor as a therapeutic target in cardiovascular disease. Platelets. 2001;12(4):197-209.
10. Moy CS, LaPorte RE, Dorman JS, et al. Insulin-dependent diabetes mellitus mortality. The risk of cigarette smoking. Circulation. 1990;82(1):37-43.
11. Barquera S, Tovar-Guzmán Vc, Campos-Nonato I, González-Villalpando C, Rivera-Dommarco J. Geography of diabetes mellitus mortality in Mexico: an epidemiologic transition analysis. Archives of medical research. 2003;34(5):407-14.
12. Group DMS. International analysis of insulin-dependent diabetes mellitus mortality: a preventable mortality perspective: the Diabetes Epidemiology Research International (DERI) Study. American Journal of Epidemiology. 1995;142(6):612-2.
13. Moghaddam MG, Ansari I, Roghani M, Moradi M. The effects of Origanum majorana on oxidative stress and histopathology of renal tissue among streptozotocin-induced diabetic rats. Thrita. 2013;2(3):29-34.
14. Diodato MD, Moon MR, Pasque MK, et al. Repair of ischemic mitral regurgitation does not increase mortality or improve long-term survival in patients undergoing coronary artery revascularization: a propensity analysis. The Annals of thoracic surgery. 2004;78(3):794-9.
15. Mihaljevic T, Lam B-K, Rajeswaran J, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. Journal of the American College of Cardiology. 2007;49(22):2191-201.
16. Kang X, Berman DS, Lewin HC, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography in patients with diabetes mellitus. American heart journal. 1999;138(6):1025-32.
17. Berman DS, Kang X, Hayes SW, et al. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men: Impact of diabetes mellitus on incremental prognostic value and effect on patient management. Journal of the American College of Cardiology. 2003;41(7):1125-33.
18. Sansanayudh N, Anothaisintawee T, Muntham D, McEvoy M, Attia J. Mean platelet volume and coronary artery disease: a systematic review and meta-analysis. International journal of cardiology. 2014;175(3):433-40.
19. Ekici B, Erkan AF, Alhan A, Sayin I, Ayli M, Töre HF. Is mean platelet volume associated with the angiographic severity of coronary artery disease? Kardiologia Polska (Polish Heart Journal). 2013;71(8):832-8.
20. Han J-Y, Choi D-H, Choi S-W, et al. Stroke or coronary artery disease prediction from mean platelet volume in patients with type 2 diabetes mellitus. Platelets. 2013;24(5):401-6.
21. Murat SN, Duran M, Kalay N, et al. Relation between mean platelet volume and severity of atherosclerosis in patients with acute coronary syndromes. Angiology. 2013;64(2):131-6.
22. Tavil Y, Sen N, Yazıcı HU, Hızal F, Abacı A, Cengel A. Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. Thrombosis research. 2007;120(2):245-50.
23. Korkmaz AN, Caliskan B, Erdem F, Caglar SO, Korkmaz U. PP-020 Evaluation of Platelet Indices as a Predictive Marker in Patients with Suspected Coronary Artery Disease Myocardial Perfusion Scintigraphy Findings. American Journal of Cardiology. 2015;115:S105.
24. Ozturk S, Gürbüz AS, Efe SÇ, et al. Association of mean platelet volume with presence of non-viable myocardium in ischaemic cardiomyopathy. Kardiologia Polska (Polish Heart Journal). 2017;75(10):1013-9.
25. Sarikaya S, Akyol L, Borekci E, et al. Mean platelet volume is associated with myocardial perfusion defect in diabetic patients: cardiovascular topic. Cardiovascular journal of Africa. 2014;25(3):110-3.
26. Sarikaya S, Sahin S, Akyol L, et al. Mean platelet volume is associated with myocardial perfusion defect in diabetic patients. Cardiovascular journal of Africa. May-Jun 2014;25(3):110-3.
27. Verberne HJ, Acampa W, Anagnostopoulos C, et al. EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision. European journal of nuclear medicine and molecular imaging. 2015;42(12):1929-40.
28. Czaja M, Wygoda Z, Duszańska A, et al. Interpreting myocardial perfusion scintigraphy using single-photon emission computed tomography. Part 1. Kardiochirurgia i torakochirurgia polska = Polish journal of cardio-thoracic surgery. Sep 2017;14(3):192-9.
29. Demirkol S, Balta S, Unlu M, et al. Evaluation of the mean platelet volume in patients with cardiac syndrome X. Clinics. 2012;67(9):1019-22.
30. Kodiatte TA, Manikyam UK, Rao SB, et al. Mean platelet volume in Type 2 diabetes mellitus. J Lab Physicians. 2012;4(1):5-9.
31. Ozturk S, Gürbüz AS, Efe SÇ, et al. Association of mean platelet volume with presence of non-viable myocardium in ischaemic cardiomyopathy. Kardiologia Polska. 2017;75(10):1013-9.
32. KARIO K, MATSUO T, NAKAO K. Cigarette smoking increases the mean platelet volume in elderly patients with risk

factors for atherosclerosis. Clinical & Laboratory Haematology. 1992;14(4):281-7.
33. Yuri Gasparyan A, Ayvazyan L, P Mikhailidis D, D Kitas G. Mean platelet volume: a link between thrombosis and inflammation? Current pharmaceutical design. 2011;17(1):47-58.
34. Kapsoritakis AN, Koukourakis MI, Sfiridaki A, et al. Mean platelet volume: a useful marker of inflammatory bowel disease activity. The American journal of gastroenterology. 2001;96(3):776-81.
35. Papanas N, Symeonidis G, Maltezos E, et al. Mean platelet volume in patients with type 2 diabetes mellitus. Platelets. 2004;15(8):475-8.
36. Hiremani M. Relation of Mean Platelet Volume with Diabetic Retinopathy in Diabetes Mellitus Type 2 Patients.
37. Rasoulinejad SA. Is there an association between mean platelet volume and diabetic retinopathy? A case-control study. Caspian J Intern Med. Mar 2021;12(2):129-34.
38. Khare M. Role of MPV in Early Diagnosis of Vascular Complication in Diabetic Patient. 2022.
39. Zheng Y-y, Wang L, Shi Q. Mean platelet volume (MPV) and platelet distribution width (PDW) predict clinical outcome of acute ischemic stroke: A systematic review and meta-analysis. Journal of Clinical Neuroscience. 2022;101:221-7.
40. Zareifar S, Farahmand Far MR, Golfeshan F, Cohan N. Changes in platelet count and mean platelet volume during infectious and inflammatory disease and their correlation with ESR and CRP. Journal of clinical laboratory analysis. 2014;28(3):245-8.
41. Schalkwijk CG, Stehouwer CD. Vascular complications in diabetes mellitus: the role of endothelial dysfunction. Clinical science. 2005;109(2):143-59.
42. Ishii H, Koya D, King G. Protein kinase C activation and its role in the development of vascular complications in diabetes mellitus. Journal of molecular medicine. 1998;76(1):21-31.
43. Hsueh WA, Anderson PW. Hypertension, the endothelial cell, and the vascular complications of diabetes mellitus. Hypertension. 1992;20(2):253-63.
44. Morrish N, Wang S-L, Stevens L, Fuller J, Keen H, Group WMS. Mortality and causes of death in the WHO Multinational Study of Vascular Disease in Diabetes. Diabetologia. 2001;44(2):S14.
45. Nitenberg A, Ledoux S, Valensi P, Sachs R, Attali J-R, Antony I. Impairment of coronary microvascular dilation in response to cold pressor–induced sympathetic stimulation in type 2 diabetic patients with abnormal stress thallium imaging. Diabetes. 2001;50(5):1180-5.
46. Slavka G, Perkmann T, Haslacher H, et al. Mean platelet volume may represent a predictive parameter for overall vascular mortality and ischemic heart disease. Arteriosclerosis, thrombosis, and vascular biology. May 2011;31(5):1215-8.
47. Alvitigala BY, Azra MAF, Kottahachchi DU, Jayasekera M, Wijesinghe R. A study of association between platelet volume indices and ST elevation myocardial infarction. International journal of cardiology. Heart & vasculature. Dec 2018;21:7-10.
48. Ding L, Sun L, Wang F, Zhu L, Zhang T, Hua F. Clinical Significance of Platelet Volume and Other Platelet Parameters in Acute Myocardial Infarction and Stable Coronary Artery Disease. Arquivos Brasileiros de Cardiologia. 2019;112:715-9.
49. Sarikaya S, Erbay AR, Sahin S, et al. Mean platelet volume is associated with myocardial perfusion defect in diabetic patients. Cardiovascular Journal of Africa. 2014;25(3):110.
50. Cabbar At, Şimşek Ma, Hünük B, Özveren O, Güzelburç Ö, Değertekin M. Evaluation Of The Relationship Between Mpv And Severity Of Coronary Artery Disease In Type 2 Diabetic Patients Without Acute Coronary Syndrome. Sdü Tıp Fakültesi Dergisi. 2021;28(3):411-7.
51. Verma N, Bhargava S, Sakrawal K, Gupta A, Grover S. An observational study of platelet parameters among patients of diabetes mellitus type 2 at Tertiary Care Centre, Udaipur. Age (Years).31(40):4.
52. Pafili K, Penlioglou T, Mikhailidis DP, Papanas N. Mean platelet volume and coronary artery disease. Curr Opin Cardiol. Jul 2019;34(4):390-8.