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Platelet index alterations in acute ST-elevation myocardial infarct: A retrospective pilot study

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ABSTRACT

Introduction: Cardiovascular diseases (CVD) are responsible for approximately 17.9 millions of deaths every year, with a higher impact on low and middle-income populations. Despite traditional risk factors, asymptomatic individuals with atherosclerosis have been identified, and new biomarkers are being sought to better predict CVD risk. This study aims to investigate the relationship between platelets indices and biochemical variability in the first day after patient admission in the hospital.

Methods: A pilot study was conducted to analyze 73 medical records of patients who experienced acute myocardial infarction, to analyze the association among mean platelet volume (MPV), platelet count (PC), creatine phosphokinase (CPK), creatine phosphokinase-MB (CKMB) and ultra-sensitive cardiac troponin I (TnI-us) between the first and second sampling (1-hour intervals), to investigate acute ST-segment elevation myocardial infarction.

Results and conclusion: The biochemical analysis showed no significant difference in CPK CK MB, TnI-us, MPV and PC levels between the first and second samples. A negative correlation between PC and MPV and a moderate negative correlation between PC and CPK were found in our AMI patients within 24 hours of hospital admission.

Keywords: cardiovascular diseases, myocardial infarct, platelet count, biomarker

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INTRODUCTION

In the contemporary scenario, cardiovascular diseases (CVD) are responsible for approximately 17.9 million deaths every year. In 2017, in Brazil, 30% of all deaths were attributed to CVD, which amounts to 383,961 cases: 1,000 deaths per day, 43 per hour, and 1 per 90 seconds. In addition, it corresponds to double the number of deaths from all types of cancer, from accidents and violence, triple the number of respiratory diseases, and six times the number of all infections, including AIDS [1].

It follows that 85% of extemporaneous deaths from CVD affect low and middle-income populations, disincented to tobacco, unhealthy diets, physical inactivity, alcohol, and environmental pollution. Even so, Fernández-Friera et al. have detected asymptomatic individuals with atherosclerosis, without traditional cardiovascular risk factors, with systemic atherosclerotic changes [2, 3]. In addition to this report, infarcted patients with a vasospastic etiology, coronary dissection or occlusion, hypercoagulable states or vasculitis are also included [4-6].

Although observational studies have established an inverse relationship between high-density lipoprotein cholesterol (HDL) and cardiovascular disease, interventions aimed at increasing HDL concentration in humans have not succeeded in reducing the risk of coronary events. Additionally, genetic variants that raise HDL levels have not been shown to lower cardiovascular risk [7]. As a result, researchers are exploring new biomarkers that can better predict the risk of ongoing cardiovascular disease, including high-sensitivity C-reactive protein (hs-CRP), carotid intima-media thickness, and coronary artery calcium score [8-10]. However, a study by Kistorp et al. found that C-reactive protein was not a reliable predictor of death or cardiovascular events in the elderly [11]. Another study by Wang et al. evaluated different biomarkers in 3209 patients over 7.4 years and found that existing biomarkers had poor accuracy in predicting the risk of events [12].

Efforts are underway to identify a widely available biomarker that can more accurately predict the risk of cardiovascular disease (CVD). Platelets (PLT) are known

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to play a pivotal role in the pathophysiology of CVD [13]. Younger platelets, which are larger and more active, promote greater platelet adhesion and aggregation, thereby increasing the risk of thrombotic vascular events [14]. As such, platelet volume serves as an indicator of platelet reactivity, and the mean platelet volume (MPV), which can be routinely obtained during complete blood count (CBC) analysis, is an accurate measure of platelet size. Numerous studies have investigated the association between MPV and the risk of coronary events, with several demonstrating a link between higher MPV and CVD risk. For instance, some studies have found that MPV is higher in patients with stable angina than in healthy individuals [15-17], while others have shown that MPV is higher in acute myocardial infarction (AMI) patients compared to those with stable angina [18]. High MPV has also been associated with poor prognosis in AMI patients [19-22]. Against this background, this study analysis aims to investigate the relationship between platelet indices and biochemical variability in first hour after hospital asmission of partients with AMI.

METHODS

Study population and design

A pilot study was conducted to analyze 73 medical records who experienced acute myocardial infarction from the Hospital Municipal de São Bernardo Campo - SP (HMSBC-SP) in the period from October 2017 to April 2018 was carried out, according to the availability of information. We compiled the variables: gender, age, mean platelet volume (MPV), platelet count (PC), creatine phosphokinase (CPK), creatine phosphokinase-MB (CKMB), and ultra-sensitive cardiac troponin I (TnI-us) between the first and second sampling, 1-hour interval. The present study aimed to investigate acute ST-segment elevation myocardial infarction (STEMI), which was defined as the presence of myocardial ischemia symptoms within 24 hours of hospital admission and troponin I levels above the 99th percentile, with a test-specific coefficient of variation. STEMI was confirmed based on either (a) ST-segment elevation of at least 1 mm in two contiguous leads or (b) presumed presence of left bundle branch block. Patients with non-cardiac complications were excluded from the analysis.

Ethical aspects

Participants were recruited at the Hospital Municipal de São Bernardo Campo - SP (HMSBC-SP). The Ethics Committee of Centro Universitário FMABC granted approval for this study (process n° 4.875.433). All participants who agreed to join the study provided written consent by signing a free and informed consent form (FICF), with thorough explanations about the adopted protocols, respecting the guidelines, regulations, and relevant ethical principles of the Declaration of Helsinki.

Biochemical and blood assays

We conducted a laboratory analysis of the cardiac enzymes CK-MB, CPK, TnI-us and cell blood count (CBC). To do so, peripheral blood was collected in a dry tube (for biochemistry tests) and K3EDTA tube (for CBC) and quantified immediately. CPK and CK-MB were analyzed by the Roche equipment Cobas Integra 400 Plus, a multiparametric automatic biochemical analysis equipment, of random access, with integrated analytical and operational units. For Troponin analysis, the HUB-QUAN PRO equipment was utilized, which is a fluorimetric immunoassay analyzer that performs quantitative measurements of biochemical markings in human blood. For platelet counting and MPV, the XN 1000 Sysmex equipment was used, where the counting was done by measuring the numbers and sizes of platelets, by hydrodynamic focusing.

Statistical analysis

Summary statistics for the obtained data were presented as mean ± standard deviation (SD) for continuous variables, and absolute and relative frequencies (%) for categorical variables. The statistical analyses were performed using GraphPad® Prism 6.0 software, with parametric variables compared using Student's t-test and non-parametric data analyzed with the Mann-Whitney test. Correlation analyses were conducted using both Spearman and Pearson's test, with a p-value less than 0.05 indicating statistical significance.

RESULTS

This pilot study included a total of 73 patients, with a gender distribution of 53% male and 47% female. The average age of the patients was 64 years. The age and gender distributions were similar in both groups.

The biochemical and platelets' variables obtained after the first and second sampling (**Table 1**) showed no statistically significant difference in terms of the variables TnI-us (ng/mL), PC (*$10^3$$mm^3$), MPV ($mcm^3$)CPK (U/L) and CKMB (U/L). (Figures 1-3)

DISCUSSION

The study included analysis of 73 medical records of patients diagnosed with AMI, with a gender distribution of 47% female and 53% male, and a mean age of 64 years. Both groups had similar distributions of age and gender. Statistically significant differences were observed in the

Table 1. Biochemical markers and platelet indices in AMI patients

	First sample	Second sample (after 1 hour)	
CPK (U/L)	553±58	667±17	p=0.52
CKMB (U/L)	74±62	63±55	p=0.29
TnI-us (ng/mL)	2.5±2.1	2.3±2.0	p=0.32
PC (*10^3mm3)	214.5±87	215±86	p=0.56
MPV (mcm3)	11±1.0	11±1.6	p=0.97

*values expressed as mean ± SD, (Mann-Whitney test)

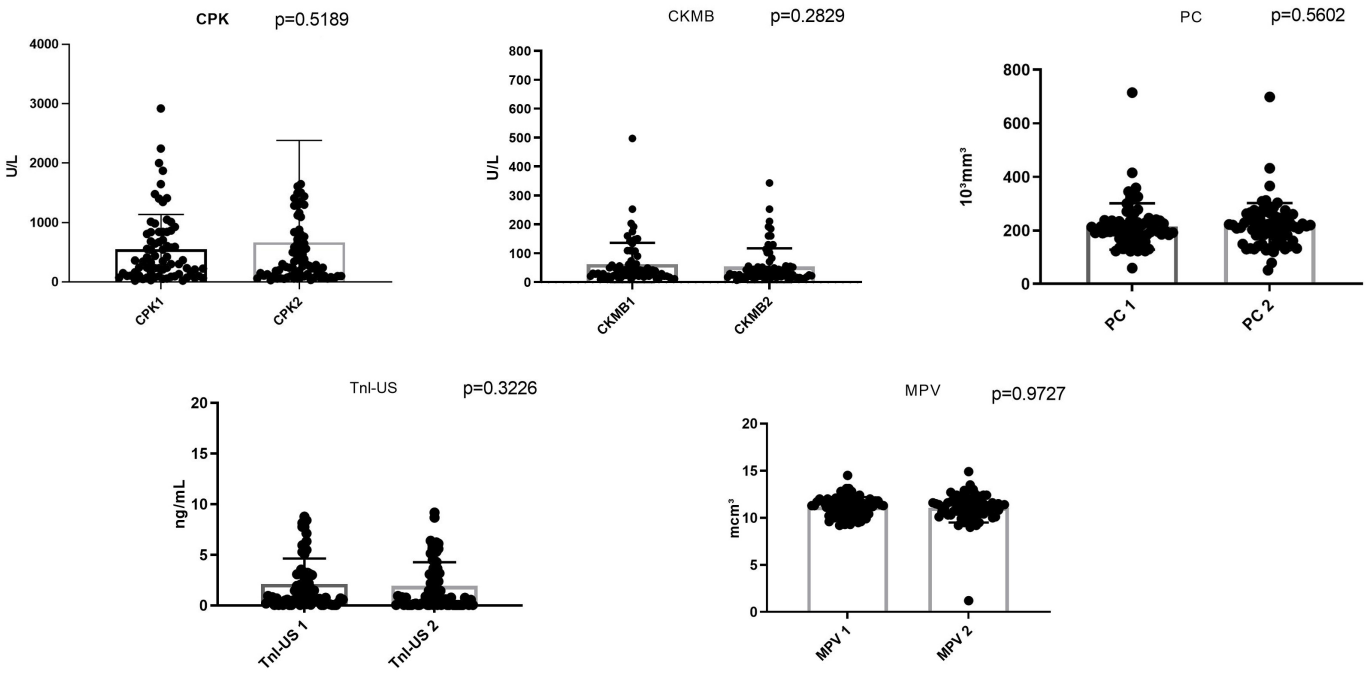

Fig. 1. Graphic representation of the absolute values of CPK (U/L), CKMB (U/L), PC (*10^3 mm3), TnI-us (µg/L) and MPV (mcm3) of the 73 patients. The values correspond to the first collection and compare with the second 1-hour interval. There was no statistically significant difference between the collections.

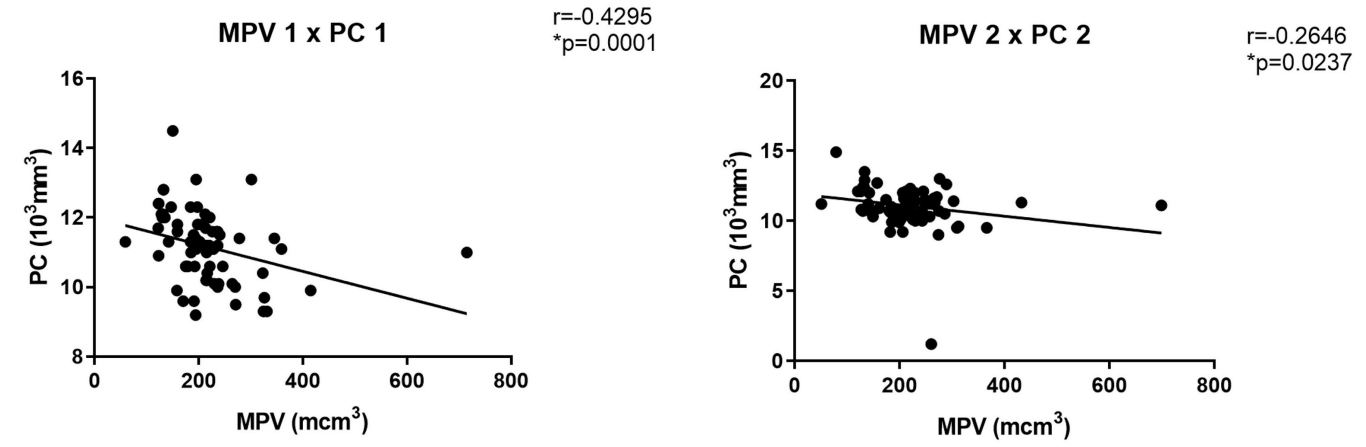

Fig. 2. Spearman's correlation between PC (*10^3 mm3) and mean platelet volume MPV (mcm3). * p<0.05. Spearman's correlation test between PC and MPV evidenced a negative correlation, denoting an inverse relationship between them. This correlation was observed in the two collections varying between the first collection (r1=-0.4295, *p<0.0001) with moderate negative correlation, and the second (r2=-0.2646, *p< 0.0237) with low negative correlation.

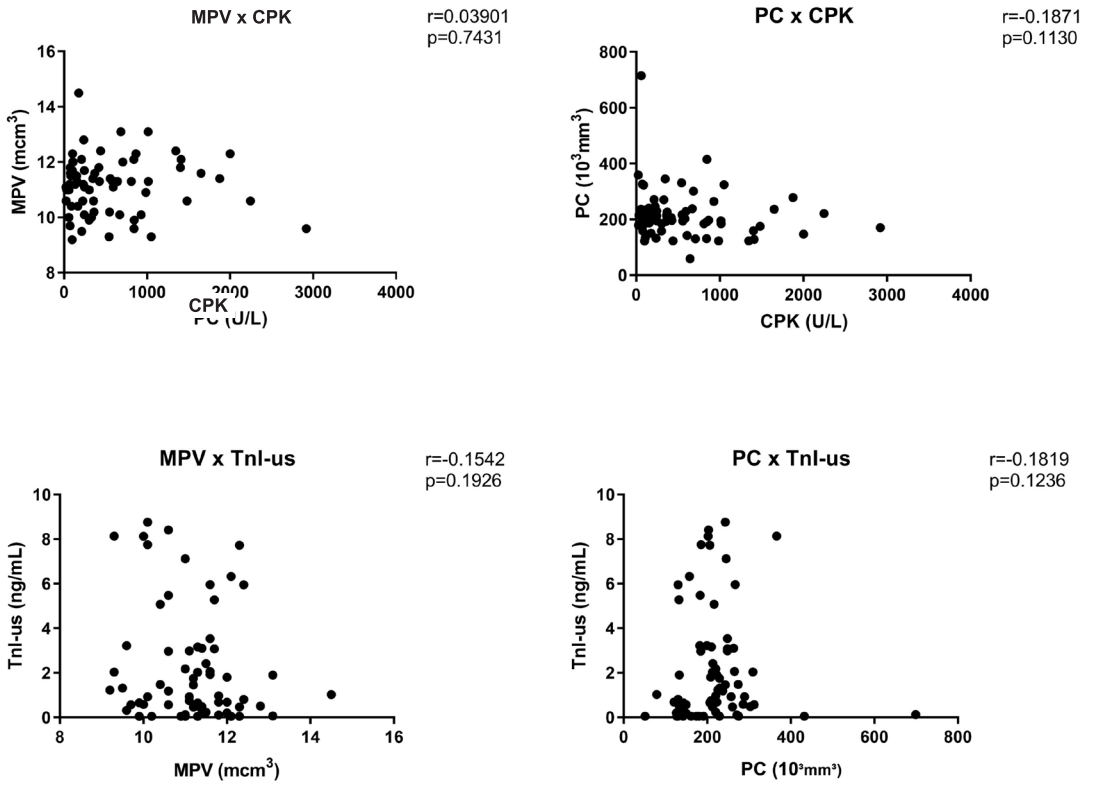

Fig. 3A. Representative of Spearman's correlation between mean platelet volume (MPV) and creatine phosphokinase (CPK); platelet (PC) and CPK, troponin I (TnI-us); mean platelet volume (MPV) and TnI-us and PC from the first collection.

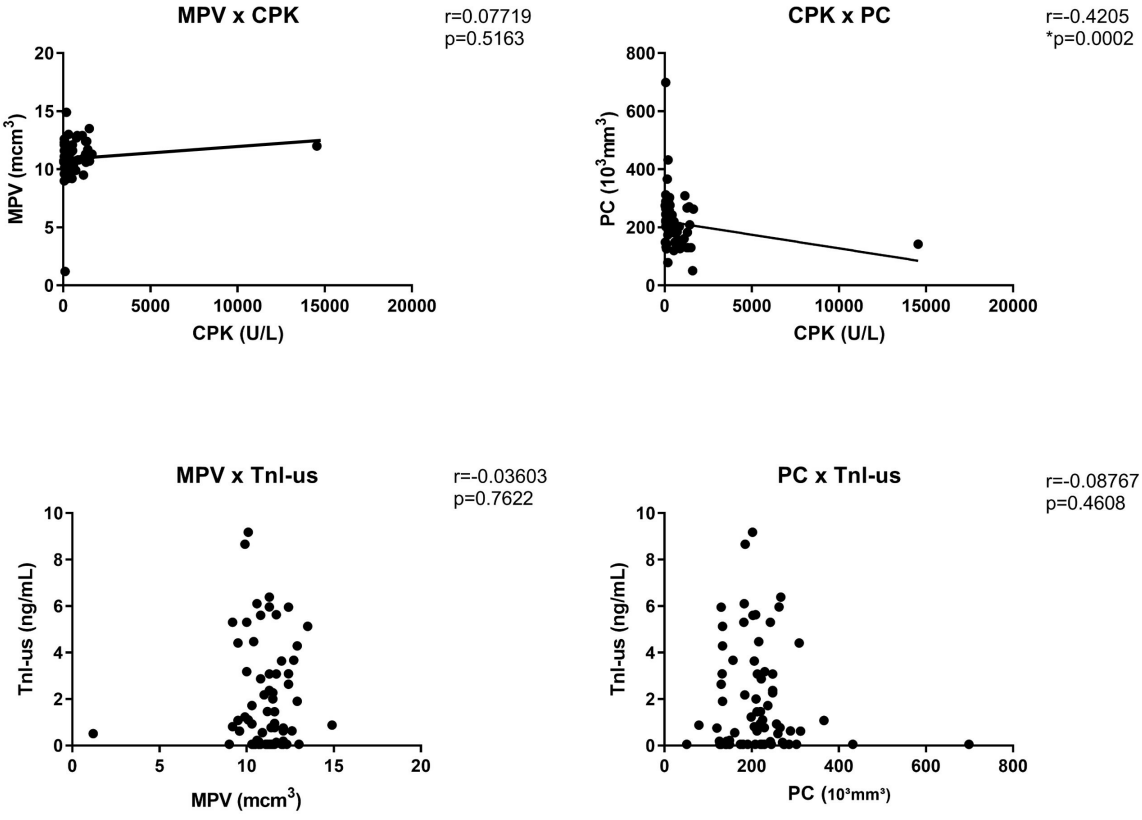

Fig. 3B. Spearman's correlation between mean platelet volume (MPV) and creatine phosphokinase (CPK), platelet (PC) and CPK, troponin I (TnI-us) and mean platelet volume (MPV) and TnI-us and PC at the second collection.

variables CK and CKMB between the first and second collection. Consistent with literature, there is evidence that maximum values of CK-MB correlate significantly with infarcted area and inversely with ventricular function. Therefore, it is proposed that peak values of CK-MB as an accurate, feasible surrogate for ventricular dysfunction and infarcted area [23]. Moreover, they have been demonstrated to be a sensitive predictor of mortality and adverse cardiac events, independent of clinical and/or angiographic factors, even after primary angioplasty [24, 25]. It is argued that there are no differences between mean TnI-us values at the 1-hour interval between collections. Despite the lack of significance between platelet count (PC) and mean platelet volume (MPV), Cameron et al. conducted a study on MPV in acute myocardial infarction (AMI) and found it to be higher than in the control group, remaining elevated during clinical follow-up ($p<0.001$) [26]. In contrast, PC was lower than in the control group ($p<0.05$) and continued to decline post-admission. Fagher et al investigated platelet count in AMI and observed a significant drop in comparison to the control group ($p<0.05$), which increased during hospitalization [27]. Martin et al. also evaluated MPV in AMI and observed a significant increase in comparison to the control group ($p<0.001$), which could be related to potential alterations in megakaryocytopoiesis (MK) and thrombopoiesis [28]. Fu et al. promoted, by coronary ligation, AMI in mice [29]. A platelet count was performed before the procedure and on the first, third and seventh days. There was a gradual increase after infarction with a peak on the third day and an increase in MPV one day later. According to a flow cytometry analysis, a significant proportion of reticulated platelets detected were found to be recently released from the bone marrow rather than the spleen. Specific techniques applied to the femur showed increased cellularity of megakaryocytes (MKs) and megakaryocyte progenitors (MKPs) on the first and third days after infarction with a significant increase of MKs and negligible increase of MKPs. This information corroborates that infarction induces proliferation and maturation of MKs. It was also observed, after the third day, that there was an elevation of pro-platelets and MKs fragments, denoting increased thrombopoiesis that follows infarction. Despite the inflammatory cascade triggered by infarction, which leads to increased expression of inflammatory cytokines, including IL-1beta, IL-6, and TNF-alpha, it has been demonstrated *in vitro* that IL-1beta and IL-6 can promote the differentiation and maturation of megakaryocytes (MKs). These results support previous studies and confirm that AMI induces development of bone marrow MKs and platelet production, which elevate in the blood. These studies suggest that after infarction both megakaryocytopoiesis and thrombopoiesis occur frequently [29,30]. In addition, Grabaovac et al. investigating the early changes in the total number of PLT and MVP in acute ischemic syndrome found biphasic changes with a decrease in the initial phase: one to three hours after hospitalization with a later increase: three to seven days after infarction. It has been suggested that platelets typically survive for around 10 days, and that 90% of these platelets are present in the bloodstream prior to the occurrence of an infarction. The analysis of the above information leads us to the contradictory, due to the non-uniformity of the appearance of immature platelets in relation to the acute event, because similar changes are observed in stable [31,32]. A negative correlation was detected between platelet count and mean platelet volume in both the first ($r1=-0.43$, $*p<0.0001$) and second collections ($r2=-0.26$, $*p<0.0237$). This correlation has previously been reported by O'Brien et al in the mid-1970s, and later confirmed by Thompson et al who observed a negative correlation ($r=-0.72$, $p<0.001$) between the two variables in a study involving 52 patients [33, 34]. Similarly, Bessman et al investigated the mean platelet volume and platelet count in 683 normal individuals and found a non-linear negative relationship between mean platelet volume and platelet count across the normal range of platelet counts [35]. This suggests that the circulating platelet mass may be a more important indicator of platelet homeostasis than platelet count or mean platelet volume alone. Additionally, it is suggested that the low correlation may be due to nonlinearity or to the one-hour interval between collections. Although there was no correlation found between mean platelet volume (MPV) and CPK and/or troponin, Taskesen et al. demonstrated that patients with high troponin levels and an MPV of 9 fl or greater had a 4.8-fold increased risk of significant obstructive coronary artery disease compared to those with normal pulse wave velocity (PWV) and high troponin levels (odds ratio 4.8, 95% confidence interval 1.31 to 17.6, $p=0.001$) [36]. In our study a moderate significant negative correlation between PC and CPK in AMI patients within 24 hours of hospital admission was observed ($r=-0.405$, $*p<0.0002$). Another study by Costa et al investigated platelet indices in 39 patients with acute myocardial infarction and found a significant positive correlation between PWV and absolute levels of CK-MB ($r=0.309$, $P<0.05$) [37]. Schultheiss et al studying 22 patients with AMI found inverse correlation ($r=-0.52$) between low platelet counts and high CK-MB values in the the non-survivors group and that this finding denoted extent of myocardial myocardial damage, furthermore, it was observed that there was a link between platelet consumption and the degree of myocardial necrosis [38].

Limitations

The study was designed as a pilot study analysis, sample size being limited.

ABREVIATIONS

AMI – Acute Myocardial infarction

CBC – Cell Blood Count

CKMB- Creatine phosphokinase-MB

CPK- Phosphokinase

CVD- Cardiovascular disease

FICF- Free and informed consent form

HDL- High-density lipoprotein cholesterol

HMSBC-SP- Hospital Municipal de São Bernardo Campo – SP

Hs-CRP- C-reactive protein

MK- Megakaryocytopoiesis

MKPS- Megakaryocyte progenitors

MKS- Megakaryocytes

MPV – Mean Platelet Volume

PC- Platelet Count

PLT- Platelets

SD- Standard deviation

STEMI- ST-segment elevation myocardial infarction

TnI-us- Troponin I ultrasensitive

AUTHORS' CONTRIBUTION

All of the authors made equal contributions to this study.

CONFLICT OF INTEREST

The authors declare that they have no competing interests. This paper received no funding.

REFERENCES

1. World Health Organization. Noncommunicable Diseases. [Internet]. 2017 [cited 2023 Mar 23]. Available from: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases
2. Fernández-Friera L, Fuster V, López-Melgar B, Oliva B, García-Ruiz JM, Mendiguren J, et al. Normal LDL-Cholesterol Levels Are Associated With Subclinical Atherosclerosis in the Absence of Risk Factors. J Am Coll Cardiol. 2017;70(24):2979-91. DOI: 10.1016/j.jacc.2017.10.024
3. Fernández-Friera L, Peñalvo JL, Fernández-Ortiz A, Ibañez B, López-Melgar B, Laclaustra M, et al. Prevalence, Vascular Distribution, and Multi-territorial Extent of Subclinical Atherosclerosis in a Middle-Aged Cohort: The PESA (Progression of Early Subclinical Atherosclerosis) Study. Circulation. 2015;131(24):2104-13. DOI: 10.1161/CIRCULATIONAHA.114.014310
4. Choudhury L, Marsh JD. Myocardial infarction in young patients. Am J Med. 1999;107(3):254-61. DOI: 10.1016/S0002-9343(99)00218-1
5. Barbash GI, White HD, Modan M, Diaz R, Hampton JR, Heikkila J, et al. Acute myocardial infarction in the young--the role of smoking. The Investigators of the International Tissue Plasminogen Activator/Streptokinase Mortality Trial. Eur Heart J. 1995;16(3):313-6.
6. Toyofuku M, Goto Y, Matsumoto T, Miyao Y, Morii I, Daikoku S, et al. Acute myocardial infarction in young Japanese women J Cardiol.1996 Dec;28(6):313-9.
7. Voight BF, Peloso GM, Orho-Melander M, Frikke-Schmidt R, Barbalic M, Jensen MK, et al. Plasma HDL cholesterol and risk of myocardial infarction: a mendelian randomisation study [published correction appears in Lancet. 2012 Aug 11;380(9841):564]. Lancet. 2012;380(9841):572-80. DOI: 10.1016/S0140-6736(12)60312-2
8. Hemingway H, Philipson P, Chen R, Fitzpatrick NK, Damant J, Shipley M, Abrams KR, et al. Evaluating the quality of research into a single prognostic biomarker: a systematic review and meta-analysis of 83 studies of C-reactive protein in stable coronary artery disease. PLoS Med. 2010;7(6): e1000286. DOI: 10.1371/journal.pmed.1000286
9. Den Ruijter HM, Peters SA, Anderson TJ, Britton AR, Dekker JM, Eijkemans MJ, et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis [published correction appears in JAMA. 2013 Oct 23;310(16):1739]. JAMA. 2012;308(8):796-803. DOI: 10.1001/jama.2012.9630
10. O'Malley PG, Taylor AJ, Jackson JL, Doherty TM, Detrano RC. Prognostic value of coronary electron-beam computed tomography for coronary heart disease events in asymptomatic populations. Am J Cardiol. 2000;85(8):945-8. DOI: 10.1016/S0002-9149(99)00906-6
11. Kistorp C, Raymond I, Pedersen F, Gustafsson F, Faber J, Hildebrandt P. N-terminal pro-brain natriuretic peptide, C-reactive protein, and urinary albumin levels as predictors of mortality and cardiovascular events in older adults. JAMA. 2005;293(13):1609-16. DOI: 10.1001/jama.293.13.1609
12. Wang TJ, Gona P, Larson MG, Tofler GH, Levy D, Newton-Cheh C, et al. Multiple biomarkers for the prediction of first major cardiovascular events and death. N Engl J Med. 2006;355(25):2631-9. DOI: 10.1056/NEJMoa055373
13. Falk E. Pathogenesis of atherosclerosis. J Am Coll Cardiol. 2006;47(8 Suppl):C7-C12. DOI: 10.1016/j.jacc.2005.09.068
14. Pereg D, Berlin T, Mosseri M. Mean platelet volume on admission correlates with impaired response to thrombolysis in patients with ST-elevation myocardial infarction. Platelets. 2010;21(2):117-21. DOI: 10.3109/09537100903487599
15. Khode V, Sindhur J, Kanbur D, Ruikar K, Nallulwar S. Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: A case control study. J Cardiovasc Dis Res. 2012;3(4):272-5. DOI: 10.4103/0975-3583.102694

16. Kiliçli-Camur N, Demirtunç R, Konuralp C, Eskiser A, Başaran Y. Could mean platelet volume be a predictive marker for acute myocardial infarction? Med Sci Monit. 2005;11(8):CR387-92.
17. Ranjith MP, Divya R, Mehta VK, Krishnan MG, KamalRaj R, Kavishwar A. Significance of platelet volume indices and platelet count in ischaemic heart disease. J Clin Pathol. 2009 Sep;62(9):830-3. DOI: 10.1136/jcp.2009.066787
18. Pizzulli L, Yang A, Martin JF, Lüderitz B. Changes in platelet size and count in unstable angina compared to stable angina or non-cardiac chest pain. Eur Heart J. 1998;19(1):80-4. DOI: 10.1053/euhj.1997.0747
19. Estévez-Loureiro R, Salgado-Fernández J, Marzoa-Rivas R, Barge-Caballero E, Pérez-Pérez A, Noriega-Concepción V, et al. Mean platelet volume predicts patency of the infarct-related artery before mechanical reperfusion and short-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Thromb Res. 2009 Nov;124(5):536-40. DOI: 10.1016/j.thromres.2009.03.012
20. Burr ML, Holliday RM, Fehily AM, Whitehead PJ. Haematological prognostic indices after myocardial infarction: evidence from the diet and reinfarction trial (DART). Eur Heart J. 1992 Feb;13(2):166-70. DOI: 10.1093/oxfordjournals.eurheartj.a060141
21. Taglieri N, Saia F, Rapezzi C, Marrozzini C, Bacchi Reggiani ML, Palmerini T, Ortolani P, et al. Prognostic significance of mean platelet volume on admission in an unselected cohort of patients with non-ST-segment elevation acute coronary syndrome. Thromb Haemost. 2011 Jul;106(1):132-40. DOI: 10.1160/TH10-12-0821
22. Goulart A, Santos IS, Sitnik D, Staniak HL, Fedeli LM, Pastore CA, et al. Design and baseline characteristics of a coronary heart disease prospective cohort: two-year experience from the strategy of registry of acute coronary syndrome study (ERICO study). Clinics (Sao Paulo). 2013;68(3):431-4. DOI: 10.6061/clinics/2013(03)RC02
23. Dohi T, Maehara A, Brener SJ, Généreux P, Gershlick AH, Mehran R, et al. Utility of peak creatine kinase-MB measurements in predicting myocardial infarct size, left ventricular dysfunction, and outcome after first anterior wall acute myocardial infarction (from the INFUSE-AMI trial). Am J Cardiol. 2015 Mar 1;115(5):563-70. DOI: 10.1016/j.amjcard.2014.12.008
24. Halkin A, Stone GW, Grines CL, Cox DA, Rutherford BD, Esente P, et al. Prognostic implications of creatine kinase elevation after primary percutaneous coronary intervention for acute myocardial infarction. J Am Coll Cardiol. 2006 Feb 21;47(4):951-61. DOI: 10.1016/j.jacc.2005.12.003
25. Chin CT, Wang TY, Li S, Wiviott SD, deLemos JA, Kontos MC, et al. Comparison of the prognostic value of peak creatine kinase-MB and troponin levels among patients with acute myocardial infarction: a report from the Acute Coronary Treatment and Intervention Outcomes Network Registry-get with the guidelines. Clin Cardiol. 2012; 35(7):424-9. DOI: 10.1002/clc.21980
26. Cameron HA, Phillips R, Ibbotson RM, Carson PH. Platelet size in myocardial infarction. Br Med J (Clin Res Ed). 1983 Aug 13;287(6390):449-51. DOI: 10.1136/bmj.287.6390.449
27. Fagher B, Sjögren A, Sjögren U. Platelet counts in myocardial infarction, angina pectoris and peripheral artery disease. Acta Med Scand. 1985;217(1):21-6. DOI: 10.1111/j.0954-6820.1985.tb01629.x
28. Martin JF, Plumb J, Kilbey RS, Kishk YT. Changes in volume and density of platelets in myocardial infarction. Br Med J (Clin Res Ed). 1983 Aug 13;287(6390):456-9. DOI: 10.1136/bmj.287.6390.456
29. Fu W, Wang J, Jiang H, Hu X. Myocardial infarction induces bone marrow megakaryocyte proliferation, maturation and platelet production. Biochem Biophys Res Commun. 2019 Mar 12;510(3):456-61. DOI: 10.1016/j.bbrc.2019.01.129
30. Ishibashi T, Kimura H, Uchida T, Kariyone S, Friese P, Burstein SA. Human interleukin 6 is a direct promoter of maturation of megakaryocytes in vitro. Proc Natl Acad Sci U S A. 1989 Aug;86(15):5953-7. DOI: 10.1073/pnas.86.15.5953
31. Sušilović Grabovac Z, Baković D, Lozo M, Pintarić I, Dujić Ž. Early Changes in Platelet Size and Number in Patients with Acute Coronary Syndrome. Int J Angiol. 2017 Dec;26(4):249-52. DOI: 10.1055/s-0037-1607048
32. Bath PM, Gladwin AM, Carden N, Martin JF. Megakaryocyte DNA content is increased in patients with coronary artery atherosclerosis. Cardiovasc Res. 1994 Sep;28(9):1348-52. DOI: 10.1093/cvr/28.9.1348
33. O'Brien JR. A relationship between platelet volume and platelet number. Thromb Diath Haemorrh. 1974 May 15;31(2):363-5. DOI: 10.1055/s-0038-1649171
34. Thompson CB, Diaz DD, Quinn PG, Lapins M, Kurtz SR, Valeri CR. The role of anticoagulation in the measurement of platelet volumes. Am J Clin Pathol. 1983 Sep;80(3):327-32. DOI: 10.1093/ajcp/80.3.327
35. Bessman JD, Williams LJ, Gilmer PR Jr. Mean platelet volume. The inverse relation of platelet size and count in normal subjects, and an artifact of other particles. Am J Clin Pathol. 1981 Sep;76(3):289-93. DOI: 10.1093/ajcp/76.3.289
36. Taskesen T, Sekhon H, Wroblewski I, Goldfarb M, Ahmad MB, Nguyen QT, et al. Usefulness of mean platelet volume to predict significant coronary artery disease in patients with non-ST-elevation acute coronary syndromes. Am J Cardiol. 2017 Jan 15;119(2):192-6. DOI: 10.1016/j.amjcard.2016.09.042
37. Costa S, Vinagre C, Chacra A, Azevedo M. Platelet indices in patients with acute coronary syndrome. J Biosci Med. 2015;3:71-6. DOI: 10.4236/jbm.2015.311009
38. Schultheiss HP, Tschoepe D, Esser J, Schwippert B, Roesen P, Nieuwenhuis HK, et al. Large platelets continue to circulate in an activated state after myocardial infarction. Eur J Clin Invest. 1994 Apr;24(4):243-7. DOI: 10.1111/j.1365-2362.1994.tb01081.x