

Potential Role of Hematological Parameters in Patients with Acute Myocardial Infarction: viewpoint

José Gildo de Moura Monteiro Júnior¹ and Dário Celestino Sobral Filho²

Pronto Socorro Cardiológico de Pernambuco (PROCAPE/UPE)¹, Recife, PE - Brazil
Universidade de Pernambuco (UPE)², Recife, PE - Brazil

Acute myocardial infarction (AMI) is one of the most important cardiovascular diseases, leading to disability and death worldwide. Atherosclerosis is the main etiology of AMI, which is characterized by a series of highly specific cellular and molecular responses that can best be described, in aggregate, as an inflammatory disease.¹ Risk factors such as arterial hypertension, diabetes mellitus, smoking, dyslipidemia, obesity, emotional stress and family history are not, in themselves, sufficient for in-hospital risk assessment of patients with AMI. Recently, several studies have found an association between oxidative stress, due to inflammation, and hypoxemia processes, with hematological changes and coronary arterial diseases, suggesting their usefulness in identifying the risk of death. These studies have shown the association of hematological parameters with prognostic biomarkers in patients with coronary artery disease.²⁻⁶ This issue of the International Journal of Cardiovascular Sciences includes the paper "Performance of a Hematological Scoring System in Predicting All-Cause Mortality in Patients with Acute Myocardial Infarction", with a proposed scoring system for in-hospital surveillance.

Several studies have shown that hypoxemia and infection are the main stimulus to differentiation processes in distinct hematological cell lines in the bone marrow, when hematological diseases, cancer, congestive heart failure, acute and chronic anemias are excluded.^{4,7} These cells originate

from a single progenitor cell called the stem cell, when for example, blood exposure to low oxygen concentrations over a long period results in differentiation and increased production of red blood cells. This stimulus to the bone marrow is produced by erythropoietin, a glycoprotein, 90% of which is produced in the kidneys, the rest being mostly formed in the liver, in response to hypoxemia. Infectious diseases cause the differentiation and final formation of specific types of leukocytes for each pathogen. Platelets have an important role in hemostasis, inflammation and innate immunity. In the last five decades, with the advent of automated counting, the hemogram was transformed into a useful clinical tool to demonstrate the daily variability in the hematopoietic response according to the patient's injury.^{7,8} In recent years, a large number of studies have provided a better knowledge of these hematological parameters, with independent information on pathophysiology and risk stratification. For example, nucleated red blood cells (NRBCs) are immature erythrocyte cells present in the bone marrow in the process of hematopoiesis. In a healthy adult, there are no NRBCs in the peripheral blood. Therefore, the presence of NRBCs in the peripheral circulation is associated with a poorer prognosis.⁹⁻¹² The neutrophil to lymphocyte ratio (NLR), a combination of two independent markers of inflammation, is considered a simple and nonspecific marker of inflammation. White blood cells, particularly lymphocytes, cause a major important modulation in the inflammatory response. Clinical and experimental

Keywords

Myocardial Infarction; Nucleated Red Blood Cells; Mean Platelet Volume; Neutrophil to Lymphocyte Ratio; Atherosclerosis; Inflammatory Diseases; Mortality.

Mailing Address: José Gildo de Moura Monteiro Júnior
Pronto Socorro Cardiológico de Pernambuco (PROCAPE)
Unidade Coronária - 1º andar
Rua dos Palmares, S/N. Postal Code: 50100-060, Santo Amaro, Recife, PE – Brazil.
E-mail: Gildo.monteiro@upe.br



José Gildo de Moura Monteiro Júnior, MD, PhD
Associate Professor Faculdade de Ciências
Médicas - FCM
Universidade de Pernambuco - UPE
Gildo.monteiro@upe.br

studies have associated lymphopenia with progressive atherosclerosis.^{13,14} Basem et al.,¹⁵ demonstrated that NLR is a strong predictor of short- and long-term mortality in stable and unstable coronary insufficiency. Patients with non-ST-segment elevation myocardial infarction with NLR >4.7 have a mortality rate of 29.8%, whereas those with NLR <3 have a mortality rate of 8.4 ($p < 0.001$).¹⁵ In another study, using a 2.54 cut-off point, NLR was a predictor of severe atherosclerosis, with a sensitivity of 74% and specificity of 53% (ROC curve 0.627; 95% CI: 0.545-0.704, $p = 0.004$).⁶ There are also studies demonstrating the association between NLR and the extent and severity of coronary artery disease.^{16,17} Large platelets are metabolically and enzymatically more active than small platelets and are characterized by an elevation in mean platelet volume (MPV). In the study by Uysal et al.,⁶ an MPV value greater than 10.4 is considered a predictor of severe atherosclerosis, with a sensitivity of 39% and specificity of 90% (ROC curve: 0.631, 95% CI: 0.549-0.708, $p = 0.003$), and can be used as a predictor and cardiac risk identifier in patients with coronary artery disease.⁶ MPV has thus been identified as an independent risk factor for acute myocardial infarction in patients with coronary artery disease.^{18,19}

Numerous other hematological parameters with prognostic markers for coronary artery disease are being studied. However, a scoring system associating NRBC, NLR and MPV represents a full blood count and its changes are related to all causes of hypoxemia and inflammation during the hospitalization of patients with

AMI, as shown in Table 1. This hematological scoring system divided the patients into two groups (low and high risk), and had a scale ranging from 0 to 49, where higher values were associated with higher risk of in-hospital death.²⁰

The potential role of an in-hospital surveillance laboratory model is feasible. However, this hematological scoring system needs to be validated with more clinical research. It is a simple and objective model, easy to interpret by all members of the multidisciplinary team and, based on evidence from existing studies, can be used for the safety of inpatients with AMI.

Author contributions

Acquisition of data: Monteiro Júnior JGM and Sobral Filho DC. Analysis and interpretation of the data: Monteiro Júnior JGM and Sobral Filho DC. Writing of the manuscript: Monteiro Júnior JGM and Sobral Filho DC. Critical revision of the manuscript for intellectual content: Monteiro Júnior JGM and Sobral Filho DC.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Table 1 – Sensitivity, specificity, positive predictive value and negative predictive value of the point scale in predicting mortality from the point scale proposed in the study.

Proposed Scale of Points	In-hospital Mortality	
	Yes	No
≥ 26 points	49	134
<26 points	6	274
Validation measures	Percentage value	CI (95%)
Sensitivity	89.1%	0.809 – 0.973
Specificity	67.2%	0.626 – 0.717
Positive predictive value	26.8%	0.204 – 0.332
Negative predictive value	97.9%	0.962 – 0.996
C Statistic	86.8%	0.818 – 0.918

CI: Confidence Interval

Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

References

- Ross R. Atherosclerosis is an inflammatory disease. *Am Heart J.* 1999;138(5 Pt 2): S419-20.
- Fuentes E, Moore-Carrasco R, Paes AMA, Trostchansky A. Role of Platelet Activation and Oxidative Stress in the Evolution of Myocardial Infarction. *J of Cardiovasc Pharmacol Ther.*2019; 24(6):509-20.
- Monteiro Júnior JGM, Torres DOC, da Silva MCFC, Martins CMH, da Silva IK, do Nascimento MEM, et al. Prognostic value of hematological parameters in patients with acute myocardial infarction: Intrahospital outcomes. *Plos One* 2018; 13(4): e0194897.
- Budziannowski J, Pieszko K, Burchardt P, Rzezniczak J, Hiczekiewicz J. The Role of Hematological Indices in Patients with Acute Coronary Syndrome. *Dis Markers.* 2017; 2017:3041565.
- Acet H, Ertaş F, Aköl MA, Oğ Z, Polat N, Bilik MZ, et al. Relationship Between Hematologic Indices and Global Registry of Acute Coronary Events Risk Score in Patients With ST-Segment Elevation Myocardial Infarction. *Clin Appl Thromb Hemost.* 2016 Jan; 22(1):60±8.
- Uysal HB, Dagli B, Akgullu C, Avcil M, Zencir C, Ayhan M, et al. Blood count parameters can predict the severity of coronary artery disease. *Korean J Intern Med.* 2016;31:1093-100.
- Monteiro Júnior JGM, de Oliveira CTD, Filho DCS. Hematological parameters as prognostic biomarkers in patients with cardiovascular diseases. *Curr Cardiol Rev.* 2019;15(4):274-82.
- Guyton AC, Hall JE. *Textbook of Medical Physiology*, 11th ed Philadelphia: Elsevier; 2006. 32: 419-28; 33: 429-38; 36: 457-68.
- Monteiro Jr JGM, Torres DOC, Silva MCFC, Ramos TMB, Alves ML, Filho WJN, et al. Nucleated red blood cells as predictors of all-cause mortality in cardiac intensive care unit patients: a prospective cohort study. *Plos One.* 2015;10(12): e0144259.
- Stachon A, Sebbers E, Holland-Letz T, Kempf R, Herinf S, Krieg M. Nucleated red blood cells in the blood of medical intensive care patients indicate increased mortality risk: A prospective cohort study. *Crit Care.* 2007;11:R62.
- Kuert S, Holland-Letz T, Friese J, Stachon A. Association of nucleated red blood cells in blood and arterial oxygen partial tension. *Clin Chem Lab Med.* 2011;49(2): 257-63.
- Desai S, Jones SL, Turner KL, Hall J, Moore LJ. Nucleated red blood cells are associated with a higher mortality rate in patients with surgical sepsis. *Surg Infect.* 2012;13(6):360-5.
- Zazula AD, Precoma-Neto D, Gomes AM, Krukliś H, Barbieri GF, Forte RY, et al. *et al.* Avaliação da relação neutrófilos/linfócitos em pacientes com suspeita de síndrome coronariana aguda. *Arq Bras Cardiol.* 2008;90(1):31-6.
- Nunez J, Nunez E, Bodi V, Sanches J. Low lymphocyte count in acute phase of ST-segment elevation myocardial infarction predicts long-term recurrent myocardial infarction. *Coron Artery Dis.*2010;21(1):1-7.
- Basem A, Zaher M, Weiserbs KF, Torbey E, Lacossiere K, Gaddam S, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short and long-term mortality after non-ST elevation myocardial infarction. *Am J Cardiol.* 2010;106(4):470-6.
- Kaya H, Ertas F, Islamoglu Y, Zekeriya K, Anturk Z, Cell H, et al. Association between neutrophil to lymphocyte ratio and severity of coronary artery disease. *Clin Appl Thromb Hemost.* 2014; 20(1): 50-4.
- Verdoia M, Barbieri L, Di Giovine G, Marino P, Suryapranata H, De Luca G, et al. Neutrophil to lymphocyte ratio and the extent of coronary artery disease: Results from a large cohort study. *Angiology* 2016; 67(1):75-82.
- Klovaite J, Benn M, Yazdanyar S, Nordestgaard BG. High platelet volume and increased risk of myocardial infarction: 39,531 participants from the general population. *J Thromb Hemost* 2011;9(1):49-56.
- Murat SN, Duran M, Kalay N, Gunebakmaz O, Akpek M, Dager L, et al. Relation between mean platelet volume and severity of atherosclerosis in patients with acute coronary syndromes. *Angiology* 2013; 64(2):131-6.
- Monteiro Jr JGM, Torres DOC, Silva MCF, Nogueira Príncipe TR, Vasconcelos RB, Brito MEC et al. Performance of a Hematological Scoring System in Predicting All-Cause Mortality in Patients with Acute Myocardial Infarction. *Int J Cardiovasc Sci.*2020 May 09. In Press.

