INTERNATIONAL JOURNAL OF
MEDICAL BIOCHEMISTRY

DOI: 10.14744/ijmb.2022.29484
Int J Med Biochem 2023;6(1):15-20

Research Article

Can additional information be obtained in the diagnosis of heart failure in type 2 diabetics by evaluating the hematological indices

Zeki Dogan[1], Hafize Uzun[2]

[1]Deparment of Cardiology, Istanbul Atlas University Faculty of Medicine, Medicine Hospital, Istanbul, Türkiye
[2]Deparment of Biochemistry, Istanbul Atlas University Faculty of Medicine, Istanbul, Türkiye

Abstract

Objectives: The aim of the present study is to investigate whether hematological indices inflammatory parameters such as neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and lymphocyte-monocyte ratio (LMR) are increased in patients with heart failure (HF) in type 2 diabetes mellitus (T2DM). It is also to compare them in diabetics without HF to investigate, whether it is important in predicting the presence of HF.

Methods: The study consisted of four subject's groups in our center between Octeber 2019 and September 2021. It recorded the laboratory results of 160 subjects of which diabetic patient without HF group (n=40), non-diabetic HF group (n=40), diabetes mellitus (DM)+HF group (n=40), and healthy controls (n=40).

Results: NLR and PLR were significantly higher, while LMR was significantly lower in all patients than controls. DM+HF group has the highest NLR (3.34±1.26), PLR (211.34±91.49), and white blood count (WBC) (9090±4834) among the groups. There was no significant difference in NLR and LMR between DM group and DM+HF group. PLR was significantly lower in non-diabetic HF than DM without HF.

Conclusion: Among these markers, NLR, PLR, and WBC could predict the presence of HF in T2DM. NLR, PLR, and WBC are independently associated with other conventional inflammatory markers as C-reactive protein levels in the early stages of HF in T2DM. Complete blood count and hematological indices can be used as additional information in terms of being non-invasive, faster, easier, and cheap in the evaluation of HF at T2DM.

Keywords: Heart failure, hematological indices, neutrophil-to-lymphocyte ratio, Type 2 diabetic

How to cite this article: Dogan Z, Uzun H. Can additional information be obtained in the diagnosis of heart failure in type 2 diabetics by evaluating the hematological indices. Int J Med Biochem 2023; 6(1):15-20.

Diabetes mellitus (DM) is a chronic metabolic disease characterized by carbohydrate, fat, and protein metabolism disorders, manifested by hyperglycemia caused by absolute or relative deficiency of insulin or insulin resistance. Chronic hyperglycemia in diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels [1].

Chronic hyperglycemia harms the human body in many different ways. One of the major injuries from hyperglycemia is injury to the vasculature, which is classified as damage to small vessels (microvascular disease) or damage to the body's large blood vessels (macrovascular disease) [2]. DM is an important cardiovascular risk factor. Diabetes is an important and independent risk factor for cardiovascular morbidity and mortality [3].

It is known that inflammation plays a very important role in the pathogenesis of cardiovascular diseases. The pathogenesis of heart failure (HF) syndrome largely involves an imbalance between inflammatory and anti-inflammatory forces [4].

Address for correspondence: Zeki Dogan, MD. Deparment of Cardiology, Istanbul Atlas University Faculty of Medicine, Medicine Hospital, Istanbul, Türkiye
Phone: +90 532 291 12 33 **E-mail:** drzeki@yahoo.com **ORCID:** 0000-0002-5620-7268
Submitted: October 14, 2022 **Revised:** October 25, 2022 **Accepted:** November 06, 2022 **Available Online:** December 09, 2023

In recent years, it has been shown that the ratios of neutrophil-to-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) may be a biomarker of systemic inflammation and are closely related to prognosis in chronic inflammatory diseases and cardiovascular diseases [4–13].

It is difficult to identify the early stages of HF development in patients with type 2 DM (T2DM), so it is crucial to identify early predictors of HF in patients with T2DM. There is not enough information in the literature on NLR, lymphocyte-monocyte ratio (LMR), and PLR, which are inflammatory markers in diabetic-HF. In this study, it was aimed the markers of inflammation (NLR, LMR, and PLR) in patients with diabetic-HF and compare them with non-HF diabetics and to investigate the relationship of these markers with each other and their value in predicting the presence of HF.

Materials and Methods

This was a retrospective study that conducted in the Atlas University Medical Faculty Medicine Hospital from Octeber 2019 to September 2021. One hundred and sixty volunteer were enrolled in the study. Our Local Ethics Committee approved the study protocol by the Declaration of Helsinki (Approval Date: August 27, 2021; number: 6985). Working groups were created as follows;

Control group (n=40)

Forty healthy (20 males and 20 females, mean age: 59.65±10.43 years) subjects who did not have any cardiac, vascular, endocrine, or inflammatory diseases with 100 mg/dL or less for fasting plasma glucose and 140 mg/dL or more for the 2nd h following a meal.

Diabetic without HF group (n=40)

Patients with T2DM (17 males and 23 females, mean age: 62.15±8.52 years) who were diagnosed in accordance with recommendations from the American Diabetes Association [14].

DM+HF group (n=40)

Forty diabetic patients with HF (medically identified as having class II-III HF, as determined by the New York Heart Association's criteria committee) in total (16 men and 24 women, mean age: 59.45±8.45 years) who exhibited a left ventricular ejection fraction <50% and were clinically stable at least 30 days were enrolled [15].

Non-diabetic HF group (n=40)

Forty patients (13 males and 27 females, mean age: 59.43±6.78 years) with HF (criteria as the previous group) were studied.

In patients who applied to our outpatient clinic with complaints of exertional dyspnea, shortness of breath at night, weakness, fatigue, anorexia, nausea, prominent neck veins, swelling in the feet and legs, coughing, and diagnosed with HF in the physical examination and clinical evaluations; teleradiogram, EKG, echocardiography examinations were ordered. Echocardiographic examinations of all patients included were performed by the same cardiologist.

Exclusion criteria

Patients under the age of 18, missing study form information or blood results, history of trauma or surgery in the past 1 month, pregnant and immunosuppressed, hematological disease, malignancy, diagnosis of acute infection, and acute or chronic lung disease were excluded from the study.

Blood samples were collected in EDTA containing tubes and anticoagulant-free tubes. After centrifugation at 5000 rpm for 15 min, the plasma and serum were divided into four aliquots. Samples were stored at –80°C until biochemical analysis.

The biochemical parameters were measured using analyzers (Roche Cobas İntegra 400, Roche Diagnostics Ltd. Germany). Serum high sensitive C-reactive protein (hs-CRP) levels were measured by nephelometry (Siemens-Dimention, Germany). Blood HbA1c was determined using a COBAS 311 analyzer using particle-enhanced immunoturbidimetric assay (Roche Diagnostics, Mannheim, Germany). Insulin levels were measured by the Cobas 8000 C702 (Roche Diagnostics, Indianapolis, IN, USA) chemistry analyzer; the result of CBC was recorded with automatic hematology analyzer (Sysmeks XN-1000, Germany). NLR, LMR, and PLR were calculated from neutrophil/lymphocyte/monocyte/thrombocyte count.

Statistical analysis

SPSS 20.0 for Windows was used to conduct statistical analysis (SPSS Inc., Chicago, IL, USA). All data were demonstrated as means ± standard deviation. The importance of group differences was evaluated using one-way ANOVA followed by post hoc Tukey test. Pearson's correlation was used to analyze the numerical data, while Spearman's correlation was employed to analyze the nominal data. A receiver operator characteristic (ROC) curve was formed and the area under the curve was used to compare the performance of various tests. The statistical significance level was set at $p<0.05$.

Results

Demographic characteristics and biochemical parameters of the patient and control groups are shown in Table 1.

The mean PLR and NLR were noticeably higher; however, LMR was significantly lower in all patients than controls. DM+HF group has the highest NLR (3.34±1.26), PLR (211.34±91.49), and white blood count (WBC) (9090±4834) among the groups. There was no statistically significant difference in the mean NLR and LMR between diabetic without HF group and DM+HF group. PLR was significantly lower in non-diabetic HF group than diabetic without HF group (Table 2).

Table 1. Demographic characteristics, and biochemical parameters of the patient and control groups

	Control (n=40)	DM (n=40)	DM+HF (n=40)	HF (n=40)
Sex				
Female	20	17	16	13
Male	20	23	24	27
Age (years)	59.7±10.4	62.2±8.5	59.5±8.5	59.4±6.8
DM duration (years)		6.32±1.87	9.85±2.82^{b***}	
BMI (kg/m^2)	25±5	29±5^{a***}	29±5^{a***}	28±6^{a**}
DBP (mmHg)	73±7	82±10^{a***}	80±11^{a***}	80±8^{a***}
SBP (mmHg)	116±9	138±16^{a***}	135±16^{a**,b***}	133±10^{a***}
Glucose (mg/dL)	81±8	197±61^{a***}	126±34^{a**,b***}	93±4^{b***,c**}
HbA1c (%)	4.80±0.49	8.48±1.21^{a***}	8.23±1.29^{a***}	5.66±0.73^{b***,c***}
Total cholesterol (mg/dL)	170±12	229±43^{a***}	208±30^{a***,b*}	198±28^{a**,b*}
HDL cholesterol (mg/dL)	53±9	50±11^{a*}	41±8^{a***,b***}	40±7^{a***,b*}
LDL cholesterol (mg/dL)	91±10	148±35^{a***}	134±37^{a***,b**}	119±35$^{a***, b***,c***}$
Triglyceride (mg/dL)	98±16	167±73^{a***}	150±45^{a***,b**}	148±47^{a***,b***}
Hs-CRP (mg/L)	0.42±0.18	0.84±0.69^{a***}	2.53±3.50^{a***,b***}	2.55±4.09^{a***,b***}

*: p<0.05; **: p<0.01; ***: p <0.001. [a]: Control; [b]: DM; [c]: DM+HF. DM: Diabetes mellitus; HF: Heart failure; BMI: Body mass index; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; HbA1c: Hemoglobin A1C; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; Hs-CRP: High sensitive C-Reactive Protein.

Table 2. The hematological indices of the patient and control groups

	Control (n=40)	DM (n=40)	DM+HF (n=40)	HF (n=40)
WBC (×10^3/mm^3)	6738±1419	6955±1772	9090±4834^{a***,b**}	6710±2000^{c***}
Platelet (×10^3/mm^3)	281±49	280±54	264±70	291±82
Neutrophil (×10^3/mm^3)	3.87±0.73	4.14±0.49^{a*}	4.22±0.50^{a*,b*}	4.87±1.69^{a***,b*,c*}
Lymphocyte (×10^3/mm^3)	2.44±0.64	1.73±0.66^{a***}	1.41±0.48^{a***,b*}	2.12±0.55^{a*,b***,c***}
Monocyte (×10^3/mm^3)	0.37±0.04	0.62±0.22^{a***}	0.52±0.11^{a***,b*}	0.55±0.18^{a***}
NLR	1.73±0.69	2.77±0.98^{a***}	3.34±1.26^{a***,b**}	2.48±1.33^{a***,c***}
LMR	6.64±1.83	3.40±2.64^{a***}	2.87±1.22^{a***,b**}	4.24±1.63^{a***,c***}
PLR	125.57±49.56	191.91±83.24^{a***}	211.34±91.49^{a***}	146.13±55.22^{a*,b***,c***}

*p<0.05; **p<0.01; ***: p<0.001. [a]: Control; [b]: DM; [c]: DM+HF. DM: Diabetes mellitus; HF: Heart failure; WBC: White blood cell; NLR: Neutrophil-lymphocyte ratio; LMR: Lymphocyte-monocyte ratio; PLR: Platelet-lymphocyte ratio.

The NLR, LMR, and PLR levels of the groups were found no correlation with any parameters including body mass index, systolic blood pressure, diastolic blood pressure, lipid, WBC, CRP, and MPV. At the same time, no correlation was found between these indices with gender and menopausal status.

The sensitivities and specificities of NLR, LMR, and PLR levels to detect HF are shown in Table 3. A ROC analysis was performed to determine the predictive power of the PLR level for the HF and showed that the PLR level of 94.47 or above had a sensitivity of 50.0%, a specificity of 85.0.

Discussion

NLR is generally accepted as an indicator of subclinical inflammation [16–19]. Recent research has revealed that NLR can be used to estimate the morbidity and mortality that may result from certain medical procedures, such angiography and appendectomy, as well as to forecast the prognosis for specific cancer kinds [20, 21]. The DM+HF group in the current study has the highest NLR, PLR, and WBC values of all the groups. PLR was significantly lower in HF than DM. The results of this study indicated that NLR and PLR might be employed as a non-invasive, readily available, affordable, and valuable indicator in clinical practice. NLR, PLR, and WBC may be considered as additional information for assessment of inflammation in HF in T2DM in clinical practice. In particular, it can be used in T2DM as the specificity of PLR (85%) is high in predicting HF.

The potential mechanisms contributing to the development of HF in T2DM patients are increasing every year. It is very important to make the diagnosis of HF in the early period when symptoms do not appear yet in terms of reducing morbidity and mortality. High values of CRP are predictive of new

Table 3. Screening efficiency of NLR, LMR, and PLR levels based on receiver-operator characteristic curve in all groups

Risk factors	AUC (95%)	Cut-off	p	Sensitivity (%)	Specifity (%)	LR+
NLR	0.247 (0.166–0.328)	1.49	0.00	50.0	74.2	19
LMR	0.744 (0.666–0.822)	3.13	0.00	62.5	74.2	2.42
PLR	0.296 (0.205–0.388)	94.47	0.00	50.0	85.0	33

NLR: Neutrophil-lymphocyte ratio; LMR: Lymphocyte-monocyte ratio; PLR: Platelet-lymphocyte ratio AUC: Area under curve.

coronary events and individuals with unstable angina and an acute myocardial infarction progressing HF [22, 23]. In almost all studies with hs-CRP, an increase in hs-CRP levels has been observed in HF of different etiologies (ischemic heart disease, idiopathic dilated cardiomyopathy, and heart valve diseases) and it has been found to be related to undesirable outcomes. In the present study, DM+HF and HF groups have the highest hs-CRP levels among the groups. According to the results of our study, CRP is an independent indicator of inflammatory activation in HF patients and T2DM. It was shown by Pandey et al. [24] that the biomarker score obtained from patients with diabetes and prediabetes can categorize the risk of HF and guide the distribution of HF protection therapies. In addition, compared to prediabetic individuals, diabetic patients exhibited a larger burden of cardiovascular risk factors, higher levels of hs-CRP, and a higher prevalence of LVH based on electrocardiography (ECG-LVH). Similar to those with normoglycemia, those with diabetes and prediabetes who had low biomarker scores also had a lower risk of HF [24]. This may indicate that inflammatory activation in HF is independent of etiology.

Some parameters such as WBC, neutrophil count, lymphocyte count, monocyte count, and NLR obtained from cheap and rapid complete blood counts in patients followed up in the emergency departments for acute HF may help in clinical decision making and in predicting the prognosis and mortality of the patients. In some studies, PLR has been shown to have superior prognostic significance than NLR. High PLR levels are a significant independent predictor of in-hospital mortality in acute coronary syndromes (ACS), according to Oylumlu et al. [25]. Patients in the lower PLR tertile group differed substantially from those in the upper PLR tertile in terms of age, the presence of DM, LVEF, and NLR levels. PLR may supplement the traditional predictors now employed in risk scoring systems to calculate the likelihood of in-hospital mortality in ACS patients [24]. In our study, among the groups, the DM+HF group has the greatest NLR. HF group has the highest neutrophil levels among the groups. It may be an independent indicator of inflammatory activation in HF, especially due to the high specificity of PLR in the study. Kalay et al. [26] grouping the patients into progressive and non-progressive illness categories based on angiography. They evaluated factors related to atherosclerosis progression. Whereas hematological factors such as MPV and WBC were associated with cardiovascular events, only increased NLR was associated with progression of atherosclerosis. NLR is also an independent predictor of thin-cap fibroatheroma [27]. Increased PLR has been shown by Kurtul et al. [28] to be an independent predictor of the incidence of more extensive coronary artery lesions in patients with ACS who had greater SYNTAX scores (SXscore). In addition, they demonstrated that PLR and SXscore might forecast in-hospital mortality in ACS patients. Greater NLR and mean platelet volume-to-lymphocyte ratio (MPVLR) on presentation in patients with acute HF were independently related with poorer cardiovascular outcomes, according to research by Angkananard et al. [29]. NLR≥3/29 and MPVLR≥8/57 were predictors for cardiovascular events and in-hospital mortality. When NLR and MPVLR were evaluated simultaneously, they performed better than when they were evaluated separately. These economical and non-invasive biomarkers ought to be regarded in the management and follow-up of patients with HF. According to Cho et al. [30], NLR is a low-cost and simple-to-apply metric that stratifies the risk of patients with acute HF and predicts short- and 3-year prognosis. Uthamalingam et al. [31] showed that higher NLR was found to have superior predictive ability for mortality than neutrophil, total WBC, and low lymphocyte count in patients with acute HF. Recent studies have shown that MLR is a significant indicator of mortality among coronary angiography patients [32]. In the present study, DM+HF group has the lowest MLR among the groups. MLR can be used to predict the presence of HF in T2DM as additional information. The study of Huang et al. [33] reported that MLR cannot be used to predict T2DM. However, MLR was a powerful independent predictor for diabetic nephropathy. High NLR, PLR, and WBC levels seem to pose a separate risk for HF.

Several limitations associated with the present study warrant mention. First, this was a retrospective and observational single-center study and our sample size is relatively small. Second, proBNP levels of the subjects were not documented.

Conclusion

It was concluded that in the absence of clinically diagnosed HF in T2DM, PLR level is increased and may serve as a diagnostic biomarker of insidious HF in T2DM. CBC and hematological indices can be used as a diagnostic tool in terms of being faster, easier, and cheap in routine testing. Additional information can be obtained by evaluating NLR, PLR, and WBC in the diagnosis of HF in T2DM. In T2DM, the roles of hematological indices in the pathogenesis of HF need to be determined by a large-scale prospective study.

Conflict of Interest: The authors declare that there is no conflict of interest.

Ethics Committee Approval: The study was approved by The Istanbul Atlas University Non-interventional Scientific Research Ethics Committee (No: 6985, Date: 27/08/2021).

Financial Disclosure: The authors declared that this study has received no financial support.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept – Z.D.; Design – Z.D.; Supervision – Z.D.; Funding – Z.D.; Materials – Z.D., H.U.; Data collection &/or processing – Z.D.; Analysis and/or interpretation – Z.D., H.U.; Literature search – Z.D., H.U.; Writing – Z.D., H.U.; Critical review – Z.D., H.U.

References

1. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2020. Diabetes Care 2020;43(Supll 1):S14–S31. [CrossRef]
2. Giri B, Dey S, Das T, Sarkar M, Banerjee J, Dash SK. Chronic hyperglycemia mediated physiological alteration and metabolic distortion leads to organ dysfunction, infection, cancer progression and other pathophysiological consequences: An update on glucose toxicity. Biomed Pharmacother 2018;107:306–28. [CrossRef]
3. Levit RD, Reynolds HR, Hochman JS. Cardiovascular disease in young women: a population at risk. Cardiol Rev 2011;19(2):60–5.
4. Oikonomou E, Tousoulis D, Siasos G, Zaromitidou M, Papavassiliou AG, Stefanadis C. The role of inflammation in heart failure: new therapeutic approaches. Hellenic J Cardiol 2011;52(1):30–40.
5. Afari ME, Bhat T. Neutrophil to lymphocyte ratio (NLR) and cardiovascular diseases: an update. Expert Rev Cardiovasc Ther 2016;14(5):573–7. [CrossRef]
6. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, et al. The relation between atherosclerosis and the neutrophil-lymphocyte ratio. Clin Appl Thromb Hemost 2016;22(5):405–11.
7. Bhat TM, Afari ME, Garcia LA. Neutrophil lymphocyte ratio in peripheral vascular disease: a review. Expert Rev Cardiovasc Ther 2016;14(7):871–5. [CrossRef]
8. Sia CH, Leow AS, Tan BY, Low CJ, Kaur R, Yeo TC, et al. The neutrophil-lymphocyte ratio and platelet-lymphocyte ratio predict left ventricular thrombus resolution in acute myocardial infarction without percutaneous coronary intervention. Thromb Res 2020;194:16–20. [CrossRef]
9. Chung J, Bae J, Kwon Y, et al. Neutrophil/Lymphocyte Ratio in Patients Undergoing Noncardiac Surgery After Coronary Stent Implantation. J Cardiothorac Vasc Anesth. 2020;34(6):1516-25.
10. Ye M, Qian X, Guo X, Wang H, Ni Q, Zhao Y, et al. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio predict severity and prognosis of lower limb arteriosclerosis obliterans. Ann Vasc Surg 2020;64:221–7. [CrossRef]
11. Afari ME, Bhat T. Neutrophil to lymphocyte ratio (NLR) and cardiovascular diseases: an update. Expert Rev Cardiovasc Ther 2016;14(5):573-7. [CrossRef]
12. Raffort J, Lareyre F. Regarding "The association between platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, and carotid artery stenosis and stroke following carotid endarterectomy". Vascular 2020;28(1):3–4. [CrossRef]
13. Szolc P, Niewiara Ł, Kawulak M, Szkodoń K, Ostrowska-Kaim E, Nosal M, et al. Neutrophıl-lymphocyte ratio and platelet-lymphocyte ratio as predıctors of coronary microcirculatory disease occurrence and outcome in patients with chronic coronary syndrome and no significant coronary artery stenosis. Wiad Lek 2020;73(12 cz 1):2598–606. [CrossRef]
14. American Diabetes Association. 2. classification and diagnosis of diabetes: Standards of medical care in diabetes-2018. Diabetes Care 2018;41(Suppl 1):S13–S27. [CrossRef]
15. The Criteria Committee of the New York Heart Association. Nomenclature and criteria for diagnosis of diseases of the heart and great vessels. 9th ed. Boston: Little, Brown & Co; 1994. p. 253–56.
16. Jilma B, Blann A, Pernerstorfer T, Stohlawetz P, Eichler HG, Vondrovec B, et al. Regulation of adhesion molecules during human endotoxemia. No acute effects of aspirin. Am J Respir Crit Care Med 1999;159(3):857–63. [CrossRef]
17. Dionigi R, Dominioni L, Benevento A, Giudice G, Cuffari S, Bordone N, et al. Effects of surgical trauma of laparoscopic vs. open cholecystectomy. Hepatogastroenterology 1994;41(5):471–6.
18. O'Mahony JB, Palder SB, Wood JJ, McIrvine A, Rodrick ML, Demling RH, et al. Depression of cellular immunity after multiple trauma in the absence of sepsis. J Trauma 1984;24(10):869–75.
19. Zahorec R. Ratio of neutrophil to lymphocyte counts- Rapid and simple parameter of systemic inflammation and stress in critically ill. Bratisl Lek Listy 2001;102(1):5–14.
20. Duffy BK, Gurm HS, Rajagopal V, Gupta R, Ellis SG, Bhatt DL. Usefulness of an elevated neutrophil to lymphocyte ratio in predicting long-term mortality after percutaneous coronary intervention. Am J Cardiol 2006;97(7):993–6. [CrossRef]
21. Tsujimura A, Kawamura N, Ichimura T, Honda K, Ishiko O, Ogita S. Telomerase activity in needle biopsied uterine myoma-like tumors: differential diagnosis between uterine sarcomas and leiomyomas. Int J Oncol 2002;20(2):361–5. [CrossRef]
22. Zebrack JS, Anderson JL, Maycock CA, Horne BD, Bair TL, Muhlestein JB; Intermountain Heart Collaborative (IHC) Study Group. Usefulness of high-sensitivity C-reactive protein in predicting long-term risk of death or acute myocardial infarction in patients with unstable or stable angina pectoris or acute myocardial infarction. Am J Cardiol 2002;89(2):145–9. [CrossRef]
23. Sanchis J, Bodí V, Llácer A, Núñez J, Facila L, Ruiz V, et al. Usefulness of C-reactive protein and left ventricular function for risk assessment in survivors of acute myocardial infarction. Am J Cardiol 2004;94(6):766–9. [CrossRef]
24. Pandey A, Vaduganathan M, Patel KV, Ayers C, Ballantyne CM, Kosiborod MN, et al. Biomarker-based risk prediction of incident heart failure in pre-diabetes and diabetes. JACC Heart Fail 2021;9(3):215–23. [CrossRef]
25. Oylumlu M, Yıldız A, Oylumlu M, Yüksel M, Polat N, Bilik MZ, et al. Platelet-to-lymphocyte ratio is a predictor of in-hospital mortality patients with acute coronary syndrome. Anatol J Cardiol 2015;15(4):277–83. [CrossRef]

26. Kalay N, Dogdu O, Koc F, Yarlioglues M, Ardic I, Akpek M, et al. Hematologic parameters and angiographic progression of coronary atherosclerosis. Angiology 2012;63(3):213–7. [CrossRef]
27. Choi YH, Hong YJ, Ahn Y, Park IH, Jeong MH. Relationship between neutrophil-to-lymphocyte ratio and plaque components in patients with coronary artery disease: virtual histology intravascular ultrasound analysis. J Korean Med Sci 2014;29(7):950–6. [CrossRef]
28. Kurtul A, Murat SN, Yarlioglues M, Duran M, Ergun G, Acikgoz SK, et al. Association of platelet-to-lymphocyte ratio with severity and complexity of coronary artery disease in patients with acute coronary syndromes. Am J Cardiol 2014;114(7):972–8. [CrossRef]
29. Angkananard T, Inthanoo T, Sricholwattana S, Rattanajaruskul N, Wongsoasu A, Roongsangmanoon W. The predictive role of neutrophil-to-lymphocyte ratio (NLR) and mean platelet volume-to-lymphocyte ratio (MPVLR) for cardiovascular events in adult patients with acute heart failure. Mediators Inflamm 2021;2021:6889733. [CrossRef]
30. Cho JH, Cho HJ, Lee HY, Ki YJ, Jeon ES, Hwang KK, et al. Neutrophil-lymphocyte ratio in patients with acute heart failure predicts in-hospital and long-term mortality. J Clin Med 2020;9(2):557. [CrossRef]
31. Uthamalingam S, Patvardhan EA, Subramanian S, Ahmed W, Martin W, Daley M, et al. Utility of the neutrophil to lymphocyte ratio in predicting long-term outcomes in acute decompensated heart failure. Am J Cardiol 2011;107(3):433–8. [CrossRef]
32. ó Hartaigh B, Bosch JA, Thomas GN, Lord JM, Pilz S, Loerbroks A, et al. Which leukocyte subsets predict cardiovascular mortality? From the LUdwigshafen RIsk and Cardiovascular Health (LURIC) Study. Atherosclerosis 2012;224(1):161–9. [CrossRef]
33. Huang Q, Wu H, Wo M, Ma J, Fei X, Song Y. Monocyte-lymphocyte ratio is a valuable predictor for diabetic nephropathy in patients with type 2 diabetes. Medicine (Baltimore) 2020;99(19):e20190.