Association of neutrophil to lymphocyte and platelets to lymphocyte ratio with the severity of coronary artery diseases in patients with diabetes mellitus

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RESEARCH PAPER

Association of neutrophil to lymphocyte and platelets to lymphocyte ratio with the severity of coronary artery diseases in patients with diabetes mellitus

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Abstract

Background: Evidence indicates an association of inflammatory process with atherosclerosis. Systemic inflammatory markers may point out the association of inflammatory changes with coronary artery diseases.

Aim: to investigate the association of Neutrophil/ Lymphocyte ratio (NLR) and Platelet/Lymphocyte Ratio (PLR) with the severity of coronary artery disease in patients with DM.

Method: We conducted a cross-sectional study of patients with coronary artery disease admitted for coronary angiography in Basra Cardiac Center. The study was done from March 2021 to February 2022. We collected demographic data, past medical history**,** biochemical tests and complete blood picture with the calculation of NLR and PLR. We reviewed coronary angiography to assess the number of diseased vessels, severity, and complexity of the lesions. The patients were divided into 2 groups; significant (≥ 70% obstruction) and non-significant CAD (< 70% obstruction).

Results: the study enrolled 228 (169 males and 59 females) patients with CAD. Significant CAD was found in 188 patients. The NLR was significantly correlated with the presence, extent, and severity of CAD (p-value 0.01, 0.003, 0.001) respectively. The PLR was significantly associated with the severity of CAD (p-value = 0.01), but non-significantly correlated with CAD presence or extent (p-value 0.28, 0.36) respectively. The NLR but not PLR was an independent marker to predict significant CAD in patients with DM.

Conclusion: neutrophil / Lymphocyte ratio was associated with the presence, extent, and severity of significant CAD in diabetic patients. Platelet/Lymphocyte Ratio was only associated with the severity of CAD.

Key words: coronary artery diseases, complete blood picture, NLR, PLR, DM.

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Introduction

Coronary artery disease (CAD) is a major risk globally and is still the first cause of disability and death, despite management advances.[1] The risk of ischaemic heart disease increases in the presence of Diabetes Mellitus (DM) which has a tremendous impact on human life and well-being.[2] About 537 million adults, aged 20-79 years, have diabetes in 2021 and expected to be 643 million in 2030 and 783 million in 2045.[3] The risk of coronary artery disease double folded with DM independent from other risk factors.[4] This can be due to lipid metabolism dysregulation, and insulin resistance, causing endothelial cell and vascular smooth muscle, altered platelet function, and abnormal

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coagulation.[5-7] The presence of other risk factors such as hypertension and obesity would exacerbate the risk of CAD.[8-9] Evidence suggests an association between atherosclerosis and chronic low-grade inflammation.[9] Neutrophils, monocytes, and lymphocytes are involved in all steps of atherosclerosis.[10,11] Neutrophils participate in the rapture of atherosclerotic plaque through releasing different enzymes, free radicals, and inflammatory factors.[12,13] Also, neutrophils promote vascular wall and reperfusion injuries by interaction with platelets and endothelial cells.[14-16] Elevated neutrophil counts can correlate with the presence and complexity of coronary atherosclerotic lesions.[17] Lymphocytes have a regulatory and immune response role to stress.[18,19] The lymphocyte count is inversely correlated with ongoing inflammation, caused by apoptosis.[20] Lower lymphocyte counts significantly correlate with the evolution of atherosclerosis.[21,22] The platelets are crucial inflammatory mediators for atherogenesis.[23] Relative thrombocytosis may result from sustained inflammation that induces platelet synthesis by enhancing megakaryocyte proliferation.[24] Activated platelets release chemokines, growth factors, and cytokines resulting in atheroembolic milieu.[25] Studies suggest that elevated platelet levels correlate with adverse cardiovascular outcomes.[26,27] Considering the role of inflammation in DM, the initiation and progression of atherosclerosis are heightened in diabetic patients.[28, 29] Recently, the Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) can be predictive and prognostic parameters in coronary artery disease with higher ratios indicating worse cardiovascular outcomes.[30,31] However, there are limited studies to assess the collective impact of NLR, PLR, and DM on patients with CAD.

The aim of this study is to investigate the association of NLR and PLR with the severity of coronary artery disease in patients with DM.

Patients and methods

A cross-sectional study was done from March 2021 to February 2022 in Basra Cardiac Center, in Basrah; southern Iraq. We collected the demographic data, past medical history, complete blood picture including measurement of NLR and PLR, and results of the coronary angiography including number of diseased vessels, severity and complexity of the lesions. Also, biochemical tests including RBS, renal function test, and any others available. We enrolled 228 patients with CAD admitted for assessment by invasive coronary angiography study. All patients provided informed consent before enrolment. Blood samples were drawn from all patients at admission and were analyzed by automated analyzers. The NLR and PLR were measured by dividing neutrophil count on lymphocyte count, and platelet count on lymphocyte count respectively. All members of the study population were divided according to the result of the coronary angiography study into 2 groups; significant (≥ 70% obstruction) and non-significant CAD (< 70% obstruction). Significant CAD is subdivided into a single vessel (SVCAD), two vessels (DVCAD), and multi-vessel CAD (MVCAD). Further subdivision was done according to severity into critical (≥7 0% obstruction) and total obstruction (100% obstruction).

Statistical analysis: The data were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 26.0. Categorical variables were summarized as numbers (N) and percentages (%), while continuous variables were summarized as mean ± standard deviations (M ±

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SD). A descriptive analysis was done, and a comparison of proportions was accomplished by using the Chi-Square test. The correlation study was done by Pearson correlation or Spearman correlation. For all tests, a P-value of < 0.05 was identified as statistically significant.

Results

The study enrolled 228 patients with coronary artery disease (males 74.1% and females 25.9%). The mean of age was 56.83 ± 11.54 years. Baseline demographic, biochemical, and hematological parameters are shown in (Table-1).

Table 1. General characteristics of the total patient population

		No. (%) or mean ± SD
Age (years)		56.83 ± 11.54
Gender	Male	169 (74.1)
	Female	59 (25.9)
BMI (kg/m^2)		26.94 ± 3.45
Index admission	Stable CAD	91 (39.9)
	UA	18 (7.9)
	NSTEMI	8 (3.5)
	STEMI	111 (48.7)
Comorbidities	DM	114 (50)
	HTN	138 (60.5)
	IHD	77 (33.8)
	Heart failure	11 (4.8)
	CVA	6 (2.6)
	AF	6 (2.6)
Dyslipidemia		42 (18.4)
Smoking	Smokers	76 (33.3)
	Non smokers	152 (66.7)
Blood pressure (mmHg)	Systolic	140.19 ± 21.46
	Diastolic	85.98 ± 11.46
Pulse rate		79.88 ± 13.43
Hemoglobin level (g/dL)		13.48 ± 1.75
WBC		10.40 ± 3.57
Neutrophil count		6.90 ± 3.45
Lymphocyte count		2.62 ± 1.28
Platelet count		255.91 ± 75.87
RBS (mg/dL)		176.97 ± 80.56
Blood urea (mg/dL)		34.82 ± 12.79
Serum creatinine (mg/dL)		0.84 ± 0.22
Duration of hospitalization (days)		1.93 ± 1.03
Complications during hospitalization	LV Dysfunction	6 (2.6)
	Arrhythmia	3 (1.3)
	No complications	219 (96.1)
Classification of CAD according to significance and extent	Significant CAD SVCAD DVCAD MVCAD Non-significant CAD	No. (%) 89 (39.04) 50(21.93) 49(21.49) 40(17.54)

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Patients with significant CAD were 188 (82.46%); including 89 (39.04%) SVCAD, 50 (21.93%) DVCAD, and 49 (21.49%) MVCAD.

The distribution of NLR and PLR values in the total patient population is shown in (Figure 1 and Figure 2) respectively.

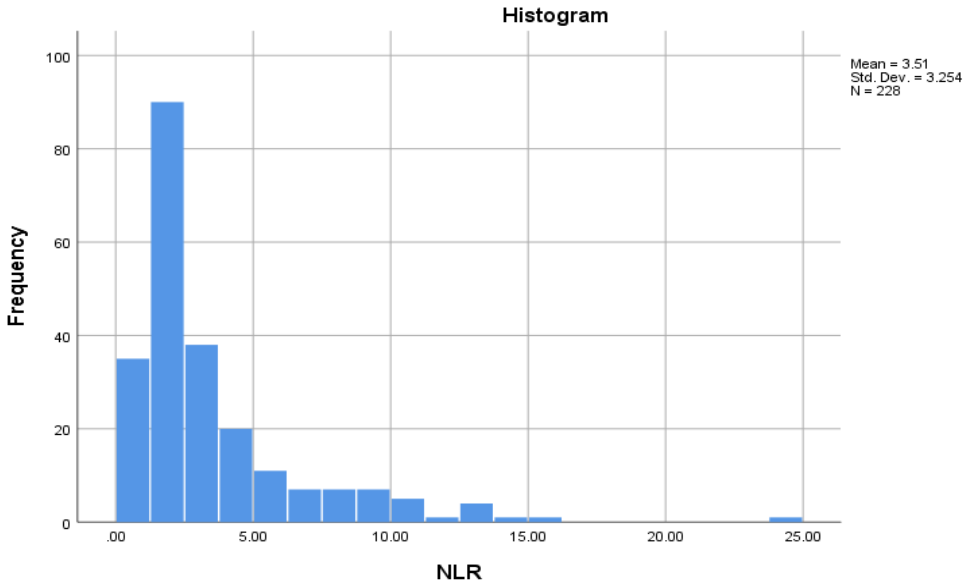

Fig 1. The distribution of NLR value in the total patient population

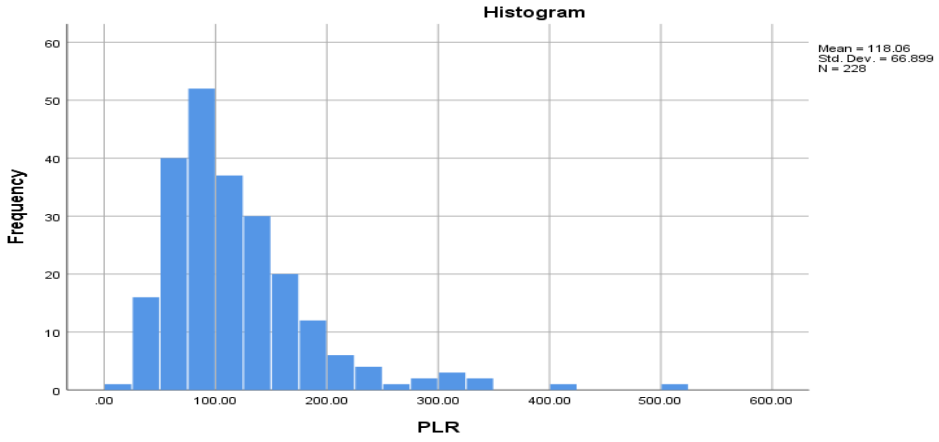

Fig 2. The distribution of PLR value in the total patient population

Comparing the correlation between NLR in patients with significant and non-significant CAD showed a significant correlation with significant obstruction. The association was positive (r = 0.16) and p-value = 0.01. There was a highly significant correlation between the NLR and the extent of CAD. The correlation was positive (r = 0.19) and the p-value = 0.003, as shown in Figure-3.

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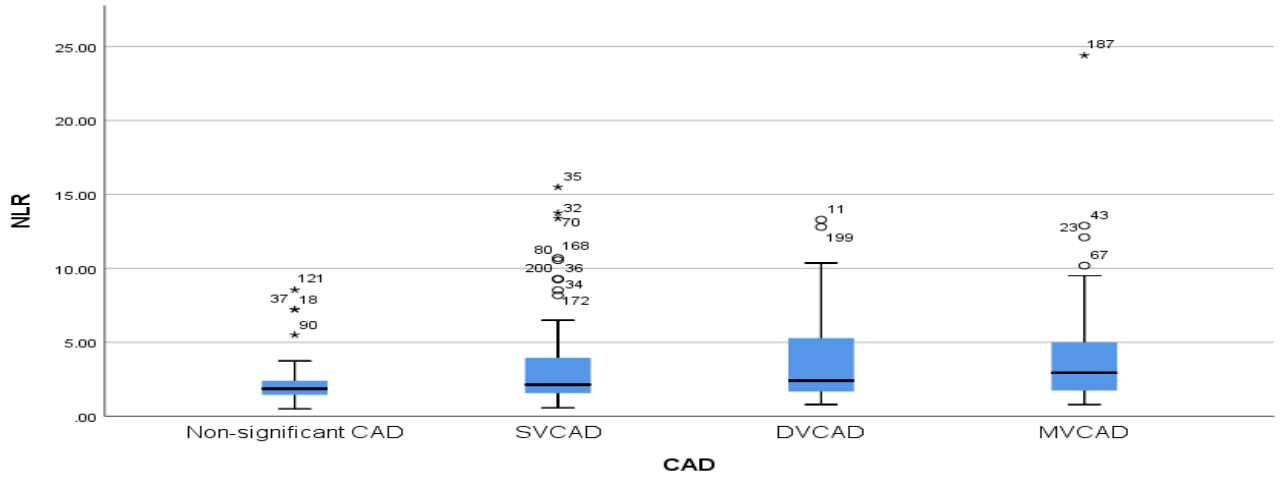

Fig 3. The NLR main distribution according to the number of obstructed coronary arteries

The correlation was highly significant between the NLR and the increasing severity of CAD. The correlation was positive (r = 0.33) and p-value = 0.001, as shown in Figure-4.

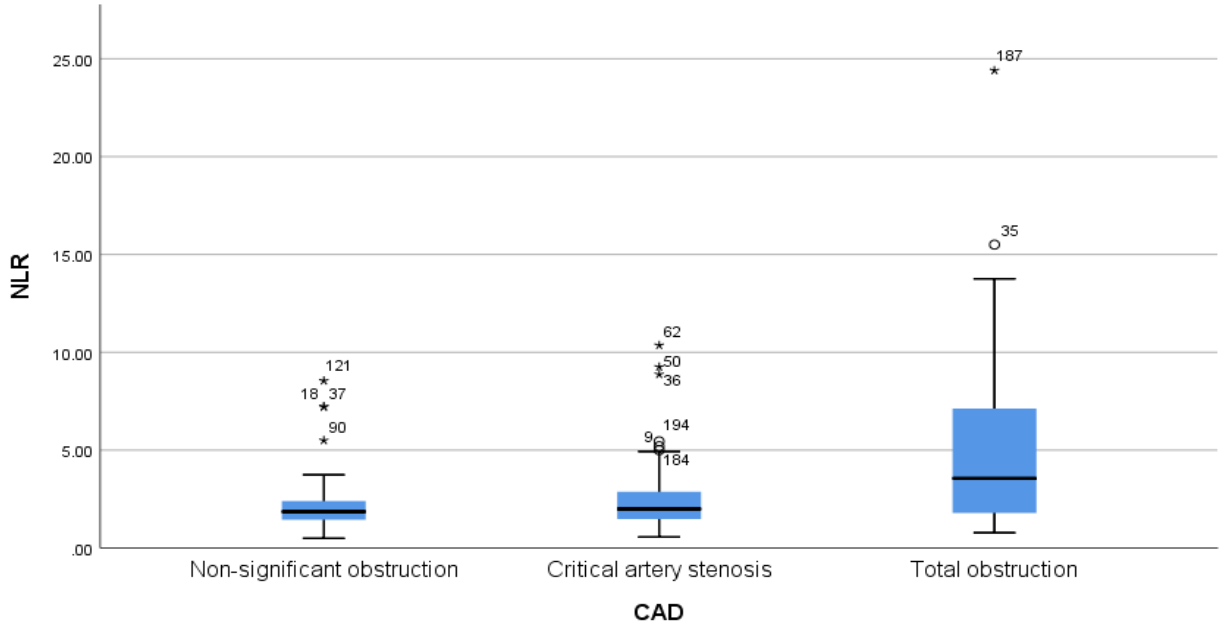

Fig 4. The NLR main distribution according to the severity of coronary artery obstruction

Comparing the correlation between PLR in patients with significant and non-significant CAD showed a non-significant correlation. The correlation was positive (r = 0.07) and p-value = 0.28. There was no significant correlation between the PLR and the extent of CAD. The correlation was positive (r = 0.06) and the p-value = 0.36, as shown in Figure-5.

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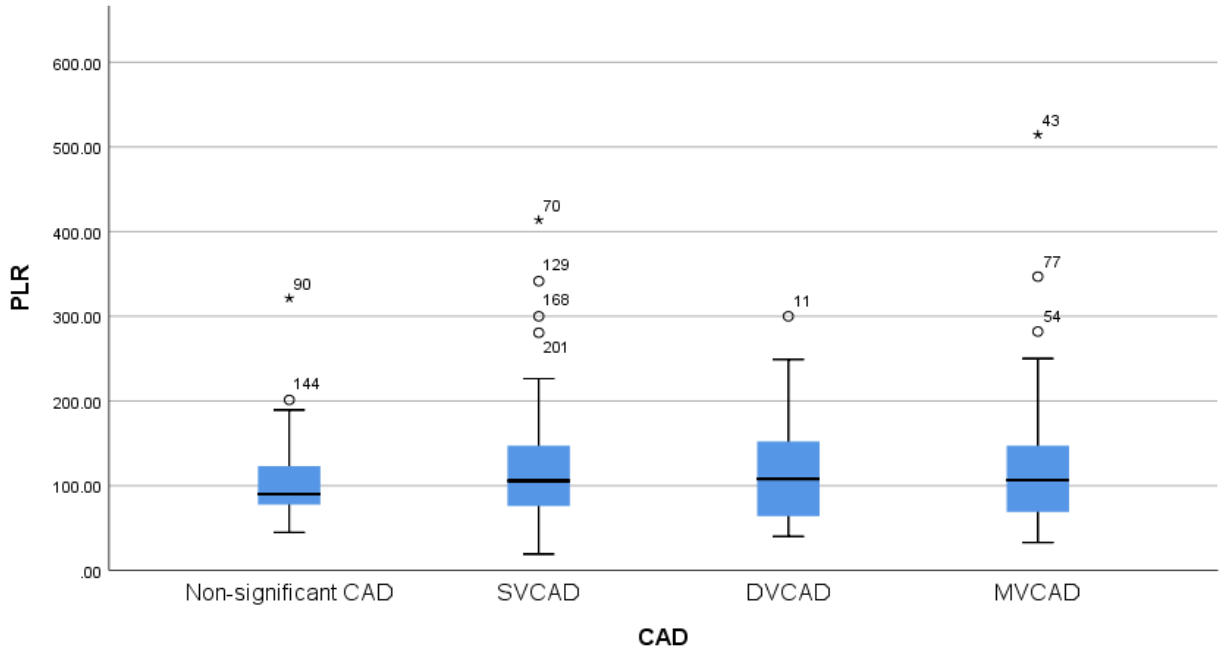

Fig 5. The PLR main distribution according to the number of obstructed coronary arteries

There was a significant correlation between the PLR and increasing severity of CAD. The correlation was positive (r = 0.15) and the p-value = 0.01, as shown in Figure-6. In logistic regression analysis, only NLR was shown to be an independent predictor of significant CAD in patients with DM.

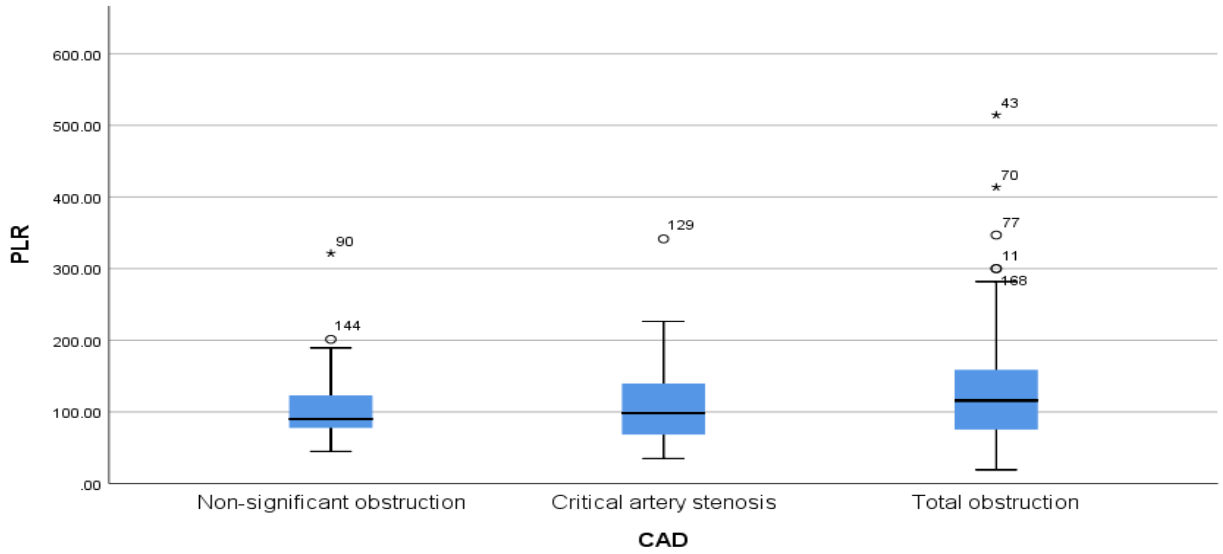

Fig 6. The PLR main distribution according to the severity of coronary artery obstruction

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Discussion

The current study showed that NLR was associated with the presence of significant CAD, which is similar to the study conducted by Mayyas FA., et al.[32] Regarding the extent of CAD, there was a highly significant correlation between the NLR and the presence of significant multi-vessel CAD which is consistent with previous studies.[33] The present study showed a highly significant correlation between the NLR and the increasing severity of CAD, the same as the result of MS H et al, [34] Regarding PLR, this study showed a significant correlation with increasing severity of CAD, a result similar to a study conducted by Reda, et al. but differs from it with respect to presence and extent.[35] Recent evidence suggests elevated levels of inflammatory markers (NLR but not PLR) associated with physiologically significant coronary lesions in patients with stable angina.[36] The relationship between elevated NLR and unstable atherosclerotic plaques has been identified in asymptomatic coronary artery disease (ACVDS).[37] In patients with Kawasaki disease, higher NLR was found to be associated with refractory disease and a higher incidence of coronary artery disease.[38] Although inflammatory markers are raised in all types of CAD, the level can be higher in acute coronary syndrome.[39,40] Furthermore, higher NLR can be a predictor of mortality in ACS patients.[41] Patients with multi-vessel disease and high NLR have higher mortality after a 2-year follow-up.[42]

In Conclusion, Patients with significant CAD had higher NLR compared to patients with non-significant CAD. Moreover, NLR was correlated with the extent and severity of CAD. The PLR was significantly correlated with the severity, but not the presence or the extent of CAD. Only NLR was an independent predictor of significant CAD.

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نسبة الخلايا البيضاء العدلة - الليمفاوية و نسبة الصفائح الدموية - الخلايا اللمفاوية كعلامات لشدة مرض الشريان التاجي في مرضى السكري

خلفيةالدراسة: تشير الأدلة إلى ارتباط العملية الالتهابية بتصلب الشرايين التاجية . قد تشير علامات الالتهاب الجهازية إلى ارتباط التغيرات الالتهابية بأمراض الشريان التاجي.

الهدف: التحقيق في ارتباط نسبة الخلايا البيضاء المعتدلة / الليمفاوية (NLR) ونسبة الصفائح الدموية / الخلايا اللمفاوية (PLR) مع شدة مرض الشريان التاجي في المرضى الذين يعانون من داء السكري

الطريقة: أجرينا دراسة مقطعية للمرضى الذين يعانون من مرض الشريان التاجي الذين تم إدخالهم لتصوير الأوعية التاجية في مركز البصرة للقلب. أجريت الدراسة في الفترة من مارس ٢٠٢١ إلى فبراير ٢٠٢٢. قمنا بجمع البيانات الديموغرافية والتاريخ الطبي السابق والاختبارات الكيميائية الحيوية وصورة الدم الكاملة مع حساب NLR نسبة الخلايا البيضاء المعتدلة الى الخلايا البيضاء اللمفاويةو كذلك نسبة الصفائح الدموية الى الخلايا البيضاء اللمفاوية بالدم PLR. قمنا بمراجعة تصوير الأوعية التاجية لتقييم عدد الأوعية المريضة وشدتها وتعقيدها لدى المرضى المصابين بالسكري ...

النتائج: شملت الدراسة ٢٢٨ (١٦٩ من الذكور و ٥٩ من الإناث) من المرضى الذين يعانون من قصور الشرايين التاجية وداء السكري. تم ملاحظة وجود مرض الشرايين التاجية في ١٨٨ مريضا. ارتبط نسبةالخلايا البيضاء المعتدلة الى الخلايا البيضاء اللمفاوية NLR بشكل كبير مع وجود ومدى وشدة تصلب الشرايين التاجية للقلب بينما ارتبط نسبة الصفائح الدموية الى الخلايا البيضاء اللمفاوية PLR بشكل كبير مع شدة مرض الشريان التاجي ولكن لم يرتبط بشكل كبير مع وجود المرض أو المدى انتشاره في الشرايين التاجية للقلب. كان NLR ولكن ليس PLR علامة مستقلة للتنبؤ بالاصابة بتصلب الشرايين التاجية في المرضى الذين يعانون من السكري.

الاستنتاج: ارتبطت نسبة العدلات / الخلايا الليمفاوية بوجود ومدى وشدة مرض الشرايين التاجية للقلب في مرضى السكري.بينما ارتبطت نسبة الصفائح الدموية / الخلايا اللمفاوية فقط مع شدة مرض الشرايين التاجية .

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