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# Correlation between Neutrophil Percentage-to-albumin Ratio and Coronary Heart Disease Complicated with Diabetes Mellitus

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**Abstract** [**Objectives**] This study was conducted to explore the relationship between neutrophil percentage-to-albumin ratio (NPAR) and coronary heart disease complicated with diabetes. [**Methods**] A total of 603 patients with coronary heart disease who underwent coronary angiography in Pingquan County Hospital from January, 2023 to December, 2023 and met the inclusion criteria were included as the research object. All the patients were divided into a coronary heart disease complicated with diabetes group (CAD + T2DM group) ($n$ = 298 cases) and a control group (CAD group) ($n$ = 305 cases), according to patients' medical history, heart color ultrasound and biochemical test results. The clinical data, biochemical test results and coronary artery imaging data of patients were recorded, and the Gensini score was calculated. The neutrophil percentage (NEUT%) and albumin count were determined to calculate NPAR. [**Results**] The NPAR value of the coronary heart disease complicated with diabetes mellitus group was (1.6 ± 0.42), which was significantly higher than that of the control group (1.47 ± 0.49), and the difference was statistically significant ($P$ < 0.05). The area under the ROC curve was 0.619 (95% *CI*: 0.591 - 0.675, $P$ < 0.05), and the prediction of coronary heart disease complicated with diabetes using NPAR showed a Youden index of 0.31, a sensitivity of 60.4%, a specificity of 40.3%, and a best cut-off score of 1.450 6. [**Conclusions**] The neutrophil percentage-to-albumin ratio (NPAR) is closely related to coronary heart disease complicated with diabetes mellitus, and NPAR has clinical application value in the diagnosis of coronary heart disease complicated with diabetes mellitus.

**Key words** Neutrophil percentage-to-albumin ratio (NPAR), Gensini score, Coronary heart disease, Coronary angiography

## 1 Introduction

Type 2 diabetes diabetes mellitus (T2DM) is the main risk factor of coronary artery disease (CAD)[1]. Studies have shown that the increase of inflammatory markers is significantly related to the severity of coronary artery disease and the increase of mortality[2]. Microcirculatory disturbance and inflammatory reaction caused by diabetes play an important role in the occurrence and development of coronary heart disease[3-4]. Coronary artery bypass grafting (CABG) is superior to percutaneous coronary intervention (PCI) in the treatment of diabetic patients with multi-vessel coronary artery disease (MVD). However, the choice of revascularization strategy should not only depend on the complexity of the disease, but also on the patient's background and complications. In addition, it is also important to carry out comprehensive risk management through drug and non-drug treatment, and it is confirmed that risk management has become an important research direction of current diagnosis and treatment strategies[5]. Neutrophil percentage-to-albumin ratio (NPAR) can more accurately measure the inflammatory reaction in blood vessels[6]. However, the relationship between NPAR and CAD complicated with T2DM is not clear. This study intended to explore the level and significance of serum neutrophil percentage-to-albumin ratio (NPAR) in CAD complicated with T2DM.

## 2 Materials and methods

**2.1 Retrospective continuous inclusion** A total of 603 patients with coronary heart disease who underwent coronary angiography in Pingquan Hospital from January, 2023 to December, 2023 and met the inclusion criteria were included as the research object. All the patients were divided into a coronary heart disease complicated with diabetes group (CAD + T2DM group) ($n$ = 298 cases) and a control group (CAD group) ($n$ = 305 cases).

**2.1.1** Inclusion criteria. (i) The condition of patients met the diagnostic criteria of coronary heart disease[7], and at least one coronary artery with a diameter of ⩾50% was confirmed by coronary angiography; and (ii) the diagnostic criteria of T2DM referred to *Clinical Guidelines for the Prevention and Treatment of Type 2 Diabetes in the Elderly in China (2022 Edition)*[8].

**2.1.2** Exclusion criteria. (i) Type 1 diabetes, special type diabetes and gestational diabetes; (ii) chest pain and precordial discomfort caused by other causes, such as aortic dissection, constrictive pericarditis or hypertrophic cardiomyopathy; and (iii) patients with hepatic and renal insufficiency. All the research subjects were required to have informed consent and approved by the Medical Ethics Committee of Pingquan Hospital.

**2.2 Collection of basic clinical data** The identification number, name, sex, age, height, weight, heart rate, blood pressure, past illness history and other basic data of all patients were recorded.

**2.3 Laboratory data determination** 2 mL of fasting blood was taken from all patients the next morning after admission, and routine biochemical tests such as blood sugar, albumin, liver and kidney function and blood lipid were carried out by a fully automatic biochemical analyzer (Beckman AU 5800) in the laboratory department of Pingquan County Hospital. The cardiac color Doppler ultrasound examination (VIVID E9 ultrasonic diagnostic instrument of GE Company, USA) was completed within 3 d after

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admission, and routine blood white blood cell and neutrophil percentage were determined with an automatic blood cell analyzer (Hyson Meikang XE2100). All the test returns were subject to routine quality control every day, and the test reports were released after double check. NPAR[9] (NPAR = neutrophil percentage-to-albumin ratio) was calculated, and a unified record of the final ratio was made.

**2.4 Evaluation of coronary artery stenosis degree** Coronary angiography is still the gold standard for the diagnosis of coronary heart disease, which is completed by two doctors in the interventional group of cardiology. The degree of stenosis in each vessel involved in coronary artery disease was quantitatively evaluated using the Gensini[10] integrating system based on the degree of stenosis at the most severe location, with a diameter $<25\%$ (1 point), $\geqslant 25\% - <50\%$ (2 points), $\geqslant 50\% - <75\%$ (4 points), $\geqslant 75\% - <90\%$ (8 points), $\geqslant 90\% - <99\%$ (16 points), and $\geqslant 99\%$ (32 points). Next, according to different coronary artery branches, the above scores were required to be multiplied by corresponding coefficients, (i) left main coronary artery disease: score $\times 5$, (ii) left anterior descending branch disease: proximal $\times 2.5$, middle $\times 1.5$, (iii) diagonal branch disease: D1 $\times 1$, D2 $\times 0.5$, (iv) left circumflex branch disease: proximal $\times 2.5$, distal $\times 1$, (v) posterior descending branch $\times 1$, (vi) posterior lateral branch $\times 0.5$, (vii) right coronary artery disease: the proximal, middle, distal and right descending branches all $\times 1$. Finally, the total score of various branches was calculated, which was the total score of the stenosis degree of coronary artery disease. A higher score indicated severer coronary artery stenosis and more complicated disease.

**2.5 Statistical methods** The data were statistically analyzed by SPSS 26.0 statistical software. Quantitative data conformed to normal distribution were represented by mean ± standard deviation ($\bar{x} \pm s$), and the comparison between two groups was made by $t$ test. Analysis of variance was used for comparison among multiple groups, and the quantitative data of skewed distribution was expressed by median interquartile range, for example, [$M$ ($Q1$, $Q3$)], and rank sum test was selected for comparison among groups. Spearman rank correlation analysis was performed on the quantitative data of skewed distribution. The qualitative data were expressed using rate or composition ratio, such as [$n$ (%)], and $\chi^2$ test was adopted. The best cut-off point for diagnosis was determined using a ROC curve. Multivariate Logistic regression was established to analyze the risk factors of coronary heart disease complicated with diabetes, with $P<0.05$ indicating a statistically-significant difference.

## 3 Results and analysis

**3.1 Baseline characteristics of two groups** As shown in Table 1, the group of coronary heart disease complicated with diabetes showed significant differences in Gensini score, WBC, HDL (mmol/L), the highest preoperative BUN, the highest preoperative uric acid (mmol/L) and blood sugar (mmol/L) between the two groups ($P<0.05$). The value of NPNR in patients with coronary heart disease and diabetes mellitus was significantly higher than that in patients with simple coronary heart disease, and the difference was statistically significant ($P<0.05$).

**Table 1 Comparison of baseline data between two groups**

| Item | CAD | CAD + T2DM | $t/Z/\chi^2$ | $P$ |
|---|---|---|---|---|
| Gender (male = 1, female = 0) | 0.59 ± 0.49 | 0.57 ± 0.50 | 0.447 886 | 0.654 413 |
| History of TIA | 0.00 ± 0.06 | 0.02 ± 0.12 | −1.430 8 | 0.153 059 |
| History of cerebral hemorrhage | 0.02 ± 0.13 | 0.01 ± 0.08 | 1.109 005 | 0.267 871 |
| History of peripheral arterial disease | 0.01 ± 0.08 | 0.01 ± 0.12 | −0.848 32 | 0.396 596 |
| History of atrial fibrillation | 0.01 ± 0.11 | 0.02 ± 0.14 | −0.673 96 | 0.500 593 |
| Current smoking//10 cigarettes/day | 0.36 ± 0.48 | 0.33 ± 0.47 | 0.802 98 | 0.422 309 |
| Heavy drinking//40 g/day | 0.18 ± 0.39 | 0.17 ± 0.38 | 0.298 563 | 0.765 379 |
| Highest BNP at admission | 0.84 ± 0.37 | 0.86 ± 0.35 | −0.429 51 | 0.667 839 |
| GENSINI score | 19.88 ± 24.38 | 24.98 ± 25.46 | −2.516 72 | <0.001 |
| LA//mm | 33.38 ± 7.30 | 34.41 ± 5.10 | −1.896 01 | 0.058 492 |
| LVEDD//mm | 48.91 ± 8.80 | 49.4 ± 6.58 | −0.730 65 | 0.465 307 |
| LVSDD//mm | 32.95 ± 8.25 | 33.49 ± 6.67 | −0.835 24 | 0.403 954 |
| EF//% | 59.78 ± 12.11 | 59.47 ± 9.81 | 0.327 077 | 0.743 736 |
| WBC//$10^9$/L | 7.21 ± 3.02 | 7.76 ± 3.28 | −2.143 41 | <0.001 |
| HGB at admission | 142.16 ± 15.33 | 140.44 ± 16.35 | 1.333 937 | 0.182 731 |
| HCT at admission//% | 42.80 ± 22.93 | 40.81 ± 4.41 | 1.469 712 | 0.142 164 |
| PLT | 221.87 ± 61.85 | 227.39 ± 70.5 | −1.024 05 | 0.306 223 |
| NPAR | 1.47 ± 0.49 | 1.60 ± 0.42 | −3.515 41 | <0.001 |
| Percentage of neutrophils//% | 0.61 ± 0.15 | 0.65 ± 0.12 | −3.997 35 | <0.001 |
| Neutrophil absolute count | 4.51 ± 2.73 | 5.11 ± 2.32 | −2.931 58 | <0.001 |
| Lymphocyte absolute count | 2.88 ± 5.13 | 2.69 ± 4.35 | 0.489 79 | 0.624 462 |

(To be continued)

(Continued)

| Item | CAD | CAD + T2DM | $t/Z/\chi^2$ | *P* |
|---|---|---|---|---|
| Monocyte absolute count | 0.50 ± 0.57 | 0.47 ± 0.39 | 0.804 939 | 0.421 173 |
| RDW-CV // % | 13.29 ± 3.42 | 12.91 ± 1.13 | 1.812 541 | 0.070 401 |
| Platelet | 0.24 ± 0.08 | 1.08 ± 13.73 | −1.069 55 | 0.285 249 |
| MPV (fl) | 10.51 ± 1.05 | 10.56 ± 0.95 | −0.614 41 | 0.539 175 |
| PDW% | 12.33 ± 1.93 | 12.54 ± 2.15 | −1.276 89 | 0.202 135 |
| TP | 72.31 ± 9.05 | 74.33 ± 44.99 | −0.766 1 | 0.443 917 |
| ALB | 43.36 ± 22.57 | 41.54 ± 4.30 | 1.367 488 | 0.171 983 |
| Total bilirubin // μmol/L | 15.13 ± 6.47 | 14.76 ± 6.29 | 0.713 441 | 0.475 85 |
| Total cholesterol // μmol/L | 4.33 ± 2.51 | 4.12 ± 1.17 | 1.288 849 | 0.197 949 |
| Triglyceride // μmol/L | 1.90 ± 2.59 | 2.21 ± 2.00 | −1.635 15 | 0.102 544 |
| HDL // mmol/L | 1.15 ± 0.34 | 1.04 ± 0.25 | 4.297 225 | <0.001 |
| LDLmax // mmol/L | 2.21 ± 0.84 | 2.15 ± 0.88 | 0.878 798 | 0.379 864 |
| CK-MB peak value // mmol/L | 24.3 ± 66.42 | 24.32 ± 59.71 | −0.004 02 | 0.996 796 |
| Highest preoperative BUN // mmol/L | 5.63 ± 1.55 | 5.96 ± 1.65 | −2.530 58 | <0.01 |
| Highest preoperative Cr value // mmol/L | 66.98 ± 15.1 | 69.04 ± 22.99 | −1.284 55 | 0.199 465 |
| Highest preoperative uric acid value // mmol/L | 328.69 ± 98.34 | 300.37 ± 83.58 | 3.777 041 | <0.001 |
| Conjugated bilirubin // mmol/L | 0.24 ± 1.36 | 0.47 ± 3.91 | −0.951 08 | 0.341 952 |
| Unconjugated bilirubin // mmol/L | 8.37 ± 7.64 | 7.64 ± 5.81 | 1.295 297 | 0.195 73 |
| Blood sugar // mmol/L | 6.37 ± 2.47 | 10.23 ± 4.55 | −12.878 2 | <0.001 |
| Highest postoperative Cr value // mmol/L | 64.76 ± 18.50 | 63.21 ± 22.59 | 0.792 858 | 0.428 281 |
| Highest postoperative uric acid value // mmol/L | 296.17 ± 91.12 | 287.05 ± 268.4 | 0.486 646 | 0.626 74 |
| Postoperative BUN // mmol/L | 6.12 ± 4.76 | 5.85 ± 2.16 | 0.784 021 | 0.433 435 |
| Lowest K value // mmol/L | 3.74 ± 0.50 | 3.74 ± 0.45 | −0.171 66 | 0.863 78 |

**3.2 Diagnostic value of NPAR in coronary heart disease complicated with diabetes** The area under the ROC curve (Fig. 1) was 0.619 (95% *CI*: 0.591 − 0.675, $P < 0.05$), and the prediction of coronary heart disease complicated with diabetes using NPAR showed a Youden index of 0.31, a sensitivity of 60.4%, a specificity of 40.3%, and a best cut-off score of 1.450 6.

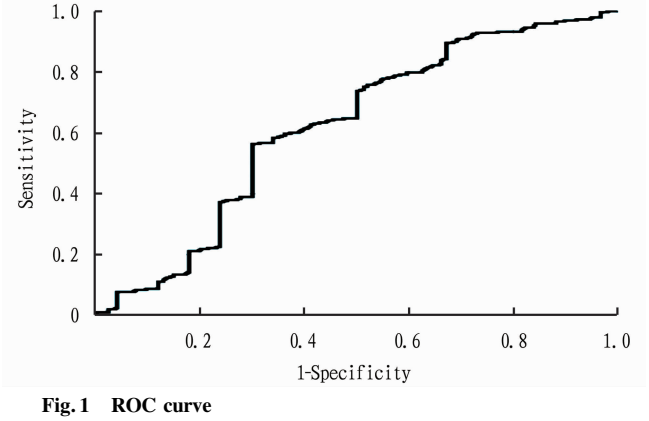



**Fig. 1 ROC curve**

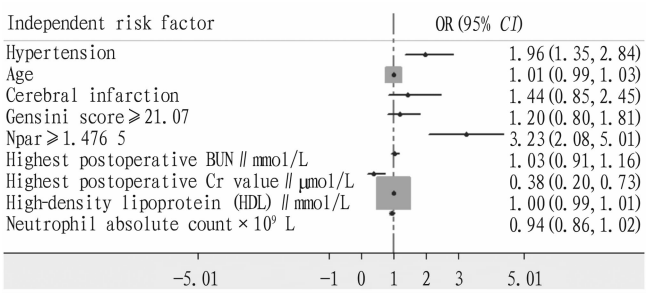
**3.3 Correlation analysis between NPAR and coronary heart disease complicated with diabetes mellitus** Correlation analysis between Gensini score and inflammatory index NPAR showed $r = 0.166$, $P < 0.01$, indicating that NPAR and Gensini score were positively correlated ($P < 0.05$).

**3.4 Logistic regression analysis of multiple risk factors** The dependent variable was whether coronary heart disease was complicated with diabetes. For the selection of independent variables, the variables undergone single factor screening $P < 0.05$ were included: hypertension, age, abnormal glucose tolerance, cerebral infarction, Gensini score median grouping (< 24.15, assigned 0; ≥24.15, assigned 1), NPAR median grouping (< 1.450 6, assigned 0; ≥1.450 6, assigned 1), highest preoperative BUN value (BUN), high-density lipoprotein (HDL), neutrophil absolute count (NEUT), and highest preoperative Cr value (Cr). Forward Conditional mode was adopted to enter models, and the binary multivariable Logistic regression models of the diabetes mellitus and coronary heart disease group and coronary heart disease group were optimized. In the models, hypertension and NPAR R≥1.450 6 were independent risk factors for coronary heart disease complicated with diabetes, and high-density lipoprotein (HDL, mmol/L) was an independent protective factor for coronary heart disease complicated with diabetes (Table 2, Fig. 2).

**Table 2 Logistic regression analysis of independent risk factors for coronary heart disease complicated with diabetes**

| Item | OR | 95% confidence interval of OR value | | *P* |
|---|---|---|---|---|
| | | Lower limit | Upper limit | |
| Hypertension | 1.961 | 1.353 | 2.841 | <0.001 * |
| Age | 1.009 | 0.988 | 1.030 | 0.407 |
| Cerebral infarction | 1.441 | 0.846 | 2.452 | 0.178 |
| GENSIN score≥24.15 | 1.202 | 0.799 | 1.810 | 0.377 |
| NPAR≥1.450 6 | 3.229 | 2.082 | 5.009 | <0.001 * |
| BUN // mmol/L | 1.028 | 0.911 | 1.160 | 0.657 |
| HDL // mmol/L | 0.380 | 0.199 | 0.726 | 0.003 # |
| Cr // μmol/L | 1.002 | 0.992 | 1.011 | 0.741 |
| NEUT // $10^9$/L | 0.938 | 0.860 | 1.023 | 0.147 |

**NOTE** * $P < 0.001$, # $P < 0.05$.




**NOTE** OR (95% *CI*) crossing 1 stands for no statistical significance, and less than 1 indicates an independent protective factor, while greater than 1 represents an independent risk factor.

**Fig. 2 Forest map of independent risk factors for coronary heart disease complicated with diabetes**

## 4 Discussion

In this study, the percentage of neutrophils and albumin in the peripheral blood of 603 patients were measured, and the ratio of them, NPAR, was calculated. It was found that the difference between the coronary heart disease group (1.47 ± 0.49) and the coronary heart disease complicated with diabetes group (1.6 ± 0.42) was statistically significant ($P < 0.001$). The latest research in the field of cardiology shows[11] that NPAR at admission is independently related to the hospitalization mortality of STEMI patients. Inflammation and dyslipidemia play a role in the pathogenesis of atherosclerosis and plaque instability. The main cause of coronary thrombosis and STEMI is the rupture of atherosclerotic plaque. Plaque rupture does not always lead to acute events because of insufficient thrombosis or insufficient lumen area to limit flow. On the contrary, the healing of plaque rupture will lead to the progression of stenosis. Hong *et al.*[12-13] reported that 69% of MI patients suffered from plaque rupture, while the proportion of SAP patients was 27%. The progression of asymptomatic diseases in mild plaques may be due to the extensive participation of serum albumin in the inflammatory reaction *in vivo*. The decrease of serum albumin will increase the poor prognosis of patients with coronary heart disease, and the decrease of serum albumin[15] will increase the risk of all-cause death of coronary heart disease. As we all know, the formation of arterial plaque is of great significance to patients with NSTEMI. Although the degree of coronary artery ischemia is similar, more and more evidence shows that inflammation and oxidative stress contribute to the development of plaque. Various inflammatory parameters are related to the formation of CCC and the prognosis of cardiovascular diseases, independent of traditional factors such as diabetes and renal insufficiency. Albumin is an important protein, which transports and binds various ions, lipids and metabolites in the body. It maintains colloid osmotic pressure and regulates the circulatory system. Hypoalbuminemia is associated with various cardiovascular diseases, including chronic and acute coronary syndrome, heart failure, hypertension, atrial fibrillation, ischemic stroke and peripheral arterial disease. In recent years, hypoproteinemia has been considered as an underestimated predictor of cardiovascular disease[14-15]. It is speculated that the increase of neutrophils or the decrease of serum albumin may be two different mechanisms leading to coronary artery disease, and they may have synergistic effects. Our statistical results show that the inflammatory factor NPAR of diabetes complicated with coronary heart disease was higher. Diabetes is one of the main reasons for increasing the incidence and mortality of coronary heart disease[16-17]. Diabetic patients present chronic inflammation and oxidative stress[18], which will aggravate the inflammatory damage of coronary artery and thus patients' condition. Therefore, NPAR was found to be a better predictor than neutrophil percentage or albumin alone.

Epidemiological data show that in angiographic studies of diabetes patients and non-diabetes patients, the number of vessels involved in coronary artery disease in diabetic patients is more than that in non-diabetes patients[19]. Correlation analysis between Gensini score and inflammatory index NPAR showed that NPAR and Gensini score were positively correlated ($P < 0.01$). A higher Gensini score indicates severer coronary artery stenosis, more complicated diseased vessel condition and higher risk, suggesting that it has potential significance for screening high-risk patients with coronary heart disease and diabetes mellitus suffering from complex vascular diseases. The binary multivariable Logistic regression model showed that the fitting of the binary multivariable Logistic regression models of the diabetes and coronary heart disease group and coronary heart disease group was optimized. In the models, hypertension and NPAR ⩾1.476 5 were independent risk factors for coronary heart disease complicated with diabetes, and high-density lipoprotein (HDL, mmol/L) was an independent protective factor for coronary heart disease complicated with diabetes, proving that NPAR has a predictive value. The area under ROC curve was 0.619 (95% CI: 0.591 − 0.675, $P < 0.05$), and the prediction of coronary heart disease complicated with diabetes using NPAR showed a Youden index of 0.31, a sensitivity of 60.4%, a specificity of 40.3%, and a best cut-off score of 1.450 6. Therefore, it could be used for predicting pathological changes.

To sum up, the ratio of neutrophils/albumin ratio (NPAR) in peripheral blood, as a new inflammatory index, is significantly related to the number of vessels with coronary artery disease and the severity of coronary artery disease, and it has certain value of assisting in judging the severity of coronary heart disease complicated with diabetes, suggesting certain clinical value.

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