Association of RLP-C and AIP with First-Onset Acute Myocardial Infarction in Young Adults: A Postprint

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Abstract

Background: Dyslipidemia is an important risk factor for the occurrence and development of acute myocardial infarction (AMI), yet AMI still occurs in some individuals with normal blood lipids. Remnant lipoprotein cholesterol (RLP-C) and atherogenic index of plasma (AIP), as non-conventional lipid indicators, have been rarely studied in relation to AMI, and their pathogenic role in young AMI patients remains unclear.

Objective: To investigate the correlation between RLP-C, AIP and first-onset acute myocardial infarction in young individuals.

Methods: A total of 1201 individuals aged 18-45 years who were admitted for initial diagnosis and underwent coronary angiography at Northern Jiangsu People' s Hospital from November 2014 to November 2021 were selected, including 627 patients with acute myocardial infarction as the study group and 574 non-acute myocardial infarction patients as the control group. General data and indicators such as triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were collected for both groups, and RLP-C and AIP were calculated according to formulas for statistical analysis. All subjects were divided into two groups based on the median age of 37 years: >37 years as Group A and $ $37 years as Group B, to analyze the risk factors for acute myocardial infarction at different age stages.

Results: The levels of RLP-C and AIP in the study group were significantly higher than those in the control group ($P<0.05$). Multivariate logistic regression analysis showed that smoking, TC, RPL-C, and AIP were all independent risk factors for acute myocardial infarction in young individuals, while HDL-C was an independent protective factor for acute myocardial infarction ($P<0.05$). In

the ROC curves of RLP-C and AIP for predicting acute myocardial infarction in the normal population, the Youden index of RLP-C was 0.547, the area under the ROC curve was 0.851 (95%CI 0.83-0.873, P<0.001), sensitivity was 84.8%, and specificity was 69.9%; the Youden index of AIP was 0.544, the area under the ROC curve was 0.813 (95% CI 0.789-0.837, P<0.001), sensitivity was 85.2%, and specificity was 66%; the combined Youden index of both indicators was 0.587, the area under the ROC curve was 0.861 (95% CI 0.840-0.882, P<0.001), sensitivity was 83.1%, and specificity was 75.6%. After stratification by age, AIP and RLP-C remained independent risk factors for acute myocardial infarction in young patients of both age groups, while HDL-C was an independent protective factor for acute myocardial infarction across different age groups.

Conclusion: RLP-C and AIP are independent risk factors for first-onset acute myocardial infarction in young populations, and their predictive value gradually increases with age; moreover, compared with traditional lipid indicators, these two indicators and their combination have greater clinical predictive value for acute myocardial infarction in young individuals.

Full Text

Clinical Study on the Predictive Effects of RLP-C and AIP on Initial Acute Myocardial Infarction in Young People

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Abstract

Background: Dyslipidemia is a well-established risk factor for acute myocardial infarction (AMI), yet AMI still occurs in individuals with normal lipid profiles. Remnant lipoprotein cholesterol (RLP-C) and the atherogenic index of plasma (AIP), as non-conventional lipid markers, have been understudied in relation to AMI, and their pathogenic role in young AMI patients remains unclear.

Objective: To investigate the correlation between RLP-C, AIP, and initial acute myocardial infarction in young individuals.

Methods: We enrolled 1,201 patients aged 18–45 years who were newly hospitalized and underwent coronary angiography at Northern Jiangsu People' s Hospital from November 2014 to November 2021. Among them, 627 patients with acute myocardial infarction constituted the study group, while 574 patients without AMI served as the control group. General clinical data and lipid parameters including triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were collected. RLP-C and AIP were calculated using standard formulas for statistical analysis. All participants were further divided into two groups based on the median age of 37 years: Group A (>37 years) and Group B ($ $37 years) to analyze risk factors for AMI across different age stages.

Results: RLP-C and AIP levels were significantly higher in the study group compared to the control group (P<0.05). Multivariate logistic regression analysis identified smoking, TC, RLP-C, and AIP as independent risk factors for AMI in young people, while HDL-C was an independent protective factor (P<0.05). ROC curve analysis for predicting AMI in the general population showed that RLP-C had a Youden index of 0.547, with an AUC of 0.851 (95%CI: 0.830–0.873, P<0.001), sensitivity of 84.8%, and specificity of 69.9%. AIP had a Youden index of 0.544, with an AUC of 0.813 (95%CI: 0.789–0.837, P<0.001), sensitivity of 85.2%, and specificity of 66%. The combined indicator showed a Youden index of 0.587, with an AUC of 0.861 (95%CI: 0.840–0.882, P<0.001), sensitivity of 83.1%, and specificity of 75.6%. After age stratification, both AIP and RLP-C remained independent risk factors for AMI in both age groups, while HDL-C was a protective factor across all ages.

Conclusion: RLP-C and AIP are independent risk factors for initial acute myocardial infarction in young people, with their predictive value increasing with age. Compared with conventional lipid markers, these two indicators—both individually and in combination—offer greater clinical predictive value for AMI in young populations.

Keywords: Young adults; Acute myocardial infarction; Remnant lipoprotein cholesterol; Atherogenic index of plasma; Coronary atherosclerosis

Introduction

Acute myocardial infarction (AMI) results from acute coronary occlusion leading to myocardial ischemia and necrosis, most commonly progressing from coronary atherosclerosis (AS). With changes in lifestyle pace and dietary patterns, the incidence of AMI is becoming increasingly prevalent among younger individuals [1]. Statistics indicate that young adults (<45 years) account for 32% of AMI patients in the past decade, compared to only about 20% in the early 21st century [2]. Abnormal lipid metabolism is widely recognized as a crucial pathogenic factor for AS, and controlling conventional lipid markers such as total cholesterol and low-density lipoprotein has become an effective preventive strategy

for high-risk populations [3]. In recent years, additional non-conventional lipid markers—including remnant lipoprotein cholesterol (RLP-C), atherogenic index of plasma (AIP), and small dense low-density lipoprotein cholesterol (sd-LDL)—have been identified as potentially closely related to AS [4-5]. To further clarify the relationship between these non-conventional lipid markers and AMI in young adults, this study retrospectively analyzed the predictive value and effects of RLP-C and AIP on the occurrence of initial acute myocardial infarction in young patients.

1.1 Study Subjects

We selected 1,201 patients aged 18–45 years who were admitted to the Department of Cardiology at Northern Jiangsu People' s Hospital with suspected coronary heart disease and underwent coronary angiography between November 2014 and November 2021. Among them, 627 patients diagnosed with acute myocardial infarction were included in the study group, while 574 patients without AMI served as the control group (including 270 individuals without coronary heart disease and 304 patients with coronary heart disease). Based on the median age of participants, they were further divided into Group A (38–45 years) and Group B (18–37 years).

Inclusion criteria: (1) Age 18–45 years; (2) Initial diagnosis of AMI meeting the guidelines established by the Chinese Society of Cardiology; (3) Completed coronary angiography, with coronary heart disease defined as $ \$50\%$ stenosis in any coronary artery or its major branches; (4) No prior use of anticoagulant or antiplatelet medications for secondary prevention of coronary heart disease.

Exclusion criteria: (1) Use of statins, fibrates, or other lipid-lowering drugs before admission; (2) Non-obstructive AMI due to myocardial bridging or coronary spasm; (3) History of old myocardial infarction, coronary artery bypass grafting, or percutaneous coronary intervention; presence of other organic heart diseases including valvular heart disease, rheumatic heart disease, dilated cardiomyopathy, or hypertrophic cardiomyopathy; (4) Comorbid malignant arrhythmia, severe cardiopulmonary insufficiency, hepatic or renal dysfunction, malignancy, connective tissue disease, hematologic disorders, trauma, or tuberculosis; (5) Patients with emotional or psychiatric disorders, depression, or inability to cooperate with the study.

1.2 Research Methods

Through the hospital medical record system, we collected baseline clinical data (personal history, family history, and past medical history) and laboratory values including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) for all

participants. RLP-C and AIP levels were calculated using the formulas: RLP-C = TC - HDL-C - LDL-C; AIP = log(TG/HDL-C). All measurements were obtained from the first blood test results within the emergency PCI treatment window after admission.

1.3 Statistical Methods

Statistical analysis was performed using SPSS 25.0. Continuous variables are presented as mean ± standard deviation, while categorical variables are expressed as rates or percentages and compared using chi-square tests. The Kolmogorov-Smirnov test was used to assess normality of continuous variables; non-normally distributed variables were compared using U-tests. After converting continuous variables to binary variables, multivariate logistic regression analysis was employed to compare the predictive effects of various lipid markers and risk factors on initial AMI in different populations, with odds ratios (OR) and 95% confidence intervals calculated. Receiver operating characteristic (ROC) curves were plotted for RLP-C, AIP, and their combination to determine optimal cutoff values for predicting initial AMI in young populations based on the Youden index. $P<0.05$ was considered statistically significant.

2.1 Comparison of Baseline Characteristics and Lipid Profiles Between Groups

The study group showed significantly higher proportions of male patients, smoking history, hypertension history, and elevated levels of TG, TC, HDL-C, LDL-C, RLP-C, and AIP compared to the control group ($P<0.05$). No statistically significant differences were observed in age, alcohol abuse history, or diabetes history between the two groups ($P>0.05$). See for details.

2.2.1 Multivariate Regression Analysis of Acute Myocardial Infarction in Young Adults

Univariate regression analysis including sex, hypertension history, smoking history, TG, TC, HDL-C, LDL-C, RLP-C, and AIP revealed all these factors as risk factors for AMI in young people. After adjusting for variables with $P<0.1$ in univariate analysis, multivariate regression analysis demonstrated that smoking history, TC, RLP-C, and AIP were independent risk factors for AMI in young adults with normal coronary arteries, with RLP-C and AIP showing stronger associations with AMI than TC. HDL-C was identified as an independent protective factor against AMI. See for details.

2.2.2 ROC Curve Analysis of RLP-C, AIP, and Combined Indicators for Predicting AMI in Young Adults

ROC curve analysis revealed that RLP-C had a sensitivity of 84.8% and specificity of 69.9%, while AIP showed a sensitivity of 85.2% and specificity of 66%. The combination of RLP-C and AIP demonstrated a sensitivity of 83.1% and specificity of 75.6%. See [Figure 1: see original paper] and .

[Figure 1: see original paper]

2.3.1 Comparison of Baseline Characteristics, Lipid Levels, AIP, and RLP-C Between Age Groups

In both age groups A and B, the study group exhibited significantly higher TG, TC, LDL-C, RLP-C, and AIP levels, and lower HDL-C levels compared to the control group ($P<0.05$). When comparing the study groups between the two age categories, Group A showed higher TG, RLP-C, and AIP levels but lower HDL-C than Group B ($P<0.05$), with no significant differences in other parameters. See .

2.3.2 Multivariate Regression Analysis of Acute Myocardial Infarction in Different Age Groups

Multivariate logistic regression analysis revealed that RLP-C and AIP remained independent risk factors for AMI in young patients across all age groups, while HDL-C was a protective factor. Notably, RLP-C and AIP showed stronger associations in Group A (38–45 years) compared to Group B (18–37 years). See .

Discussion

Our findings demonstrate that after adjusting for confounding factors such as sex, hypertension, and smoking history, both RLP-C and AIP are independent risk factors for initial AMI in young adults, while HDL-C is an independent protective factor. Further age-stratified analysis revealed that RLP-C and AIP showed stronger correlations with AMI incidence in patients aged 37–45 years compared to those aged 18–37 years. Additionally, among non-AMI controls, RLP-C levels were higher in the 38–45 age group than in the 18–37 group. These results suggest that RLP-C and AIP pose greater risks for young AMI patients compared to conventional lipid markers and may also indicate risk in young individuals with normal coronary arteries, making them powerful predictive indicators for AMI.

RLP-C represents cholesterol-rich particles derived from chylomicrons (CM) and very low-density lipoproteins (VLDL) after lipolysis by lipoprotein lipase (LPL), transforming into small particles rich in triglycerides, cholesterol, cholesterol esters, and apolipoprotein E (apoE) [6]. In clinical practice, RLP-C measurement standards have been difficult to unify due to varying detection methods, limiting its widespread application. The Verbo A formula commonly used in China calculates RLP-C as: RLP-C = TC - HDL-C - LDL-C [7]. RLP-C demonstrates strong atherogenic potential comparable to LDL-C. Despite its larger size, it can penetrate coronary endothelium through multiple pathways to form foam cells. Moreover, with triglyceride content nearly 40 times that of LDL, RLP-C can extensively bind to proteoglycans on monocytes, bypassing oxidation and acetylation processes to more readily form foam cells [8-9]. Additionally, CM remnants in RLP-C contain lysophosphatidylcholine, which is highly homologous to oxidized LDL (Ox-LDL) and can induce monocyte chemoattractant protein-1 expression and regulate early growth response factor-1 (Egr-1) in vascular smooth muscle cells, thereby affecting coronary endothelial function [10].

The atherogenic index of plasma (AIP), proposed by Dobiásová, serves as a concept to estimate sd-LDL levels, calculated as the logarithm of the TG/HDL-C ratio. This value inversely correlates with sd-LDL particle size and effectively reflects sd-LDL concentration [11]. sd-LDL particles, defined as LDL with mean diameter <25.5 nm, possess unique physicochemical properties that enhance their atherogenic potential [12]. Their smaller size increases arterial wall permeability, while reduced recognition by LDL receptors prolongs plasma half-life [13]. Furthermore, sd-LDL is more susceptible to qualitative modifications including oxidation, desialylation, and glycation due to weaker antioxidant capacity [14]. Oxidized sd-LDL exhibits increased affinity for intimal proteoglycans and is preferentially taken up by macrophages to form foam cells [15-16]. It also impairs endothelium-dependent vasodilation, promotes endothelial dysfunction, and reduces the barrier function against inflammatory factors [17]. Recent studies have confirmed AIP as an independent risk factor for premature coronary artery disease with predictive value for coronary lesions in young populations [18].

HDL-C has long been recognized as a cardiovascular protective factor, with each 1 mg/ml increase corresponding to a 3% reduction in cardiovascular risk. It promotes reverse cholesterol transport and excretion while exerting anti-inflammatory and antioxidant effects on coronary arteries [19-20]. Previous studies have shown that medications increasing HDL levels (such as niacin and cholesterol ester transfer protein inhibitors) can reduce residual cardiovascular risk to varying degrees [21]. Our study similarly identified HDL-C as a protective factor against initial myocardial infarction in young adults. In comparisons between control groups of different ages, patients aged 38–45 showed higher AIP and RLP-C levels than those aged 18–37, though the magnitude of increase was modest, possibly due to the protective effects of relatively higher HDL-C levels in individuals with normal coronary arteries—an area requiring further investigation.

In summary, RLP-C and AIP serve as independent risk factors for AMI in young adults and can be used as predictive indicators. These findings suggest that cardiologists should monitor these non-conventional markers in addition to conventional lipid parameters, potentially providing new therapeutic targets for preventing AMI in young populations.

As a retrospective study with limited sample size and potential selection bias, larger prospective studies are needed to validate these findings.

Author Contributions

DENG Yifan contributed to study conception, design, feasibility analysis, and manuscript writing. ZHU Mixue, LIU Juan, and NIE Ri performed data collection, collation, and statistical analysis. HE Shenghu and ZHANG Jing revised the manuscript. ZHANG Jing was responsible for quality control, final approval, overall supervision, and project administration.

Conflict of Interest

This is a retrospective study with no conflicts of interest to declare.

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Note: Figure translations are in progress. See original paper for figures.