Relationship between non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio and coronary heart disease

Ya Li*, Shu Li*, Yulin Ma, Jialing Li, Mingying Lin, Jing Wan

Objective **To investigate the association between non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio and degree of coronary artery stenosis proven by coronary angiography.**

Methods **A total of 1867 patients were enrolled into this study and analyzed retrospectively. Three hundred eighty-five non-coronary artery disease hospitalized patients were selected as control group, 1482 patients diagnosed as coronary artery disease were classified into three subgroups according to the tertiles of their SYNTAX score. We compared the level of non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio among the three subgroups. The Spearman correlation was used to analyze the correlation between non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio and SYNTAX, logistic regression was used for analyzing independent predictors of coronary artery disease.**

Results **The level of non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio was higher in coronary artery disease group compared with non-coronary artery disease group ($P < 0.01$). The Spearman correlation analysis showed that non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio were significantly correlated with SYNTAX score ($r = 0.081$, $P < 0.001$; $r = 0.216$, $P < 0.001$). In multivariate logistic regression analysis showed that non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio were independent predictors of coronary artery disease (odds ratio = 3.645, 95% confidence interval, 1.267–10.486; OR = 2.096, 95% confidence interval, 1.438–3.054).**

Conclusion **Non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio were associated with the severity of coronary artery lesions,which can be used as a biomarker for the evaluation of severity of coronary artery disease.**

Coronary Artery Disease 2020, **31**:623–627

Keywords: coronary artery disease, monocyte/high-density lipoprotein cholesterol ratio, non–high-density lipoprotein cholesterol/apolipoprotein A-I ratio

From the Department of Cardiology, Zhongnan Hospital of Wuhan University, Wuhan, China

Correspondence to Jing Wan, MD, Department of Cardiology, Zhongnan Hospital of Wuhan University, No. 169 Donghu Road, Wuchang District, Wuhan 430071, Hubei Province, China
Tel: +86 027 67813477; fax: +86 027 6781 3477; e-mail: wanjing_zn@163.com

*Y.L. and S.L. contributed equally to the writing of this article.

Received 12 November 2019 **Accepted** 28 December 2019

Introduction

Coronary artery disease (CAD) is one of the most common diseases that endanger human health, which affects patients' quality of life and long-term prognosis. Many factors contribute to the occurrence and the development of CAD. Atherosclerosis is the main cause of coronary heart disease. Inflammation, oxidative stress, and endothelial dysfunction are considered to be the main mechanisms of atherosclerosis. And inflammation plays an important role throughout the process of atherosclerosis [1]. Non–high-density lipoprotein cholesterol (non-HDL-C) is the sum of all atherogenic cholesterol in serum, as proposed by the Third Report of The National Cholesterol Education Program, reducing non-HDL-C is the second goal of treatment in the process of antiatherosclerosis [2]. Previous studies have shown that non-HDL-C is associated with the risk of coronary heart disease [3,4]. The protein component of HDL-C is 70% apolipoprotein A-I (apoA-I) and 20% apolipoprotein A-II (apoA-II) [5], which has been shown to play a role in anti-inflammation and antioxidation, has the effect of protecting vascular endothelial cell, nitric oxide production, expressions of inflammatory mediators, and endothelial progenitor cell proliferation [6,7]. Monocytes and macrophages are the main proinflammatory cells in the formation of atherosclerosis, which could secret inflammatory factors involved in the formation of atherosclerosis [8]. In recent years, researches on inflammatory biomarkers related to atherosclerosis have become a hot topic, based on the role of non-HDL-C, HDL-C, and monocytes in the atherosclerosis process. Clinicians pay

DOI: 10.1097/MCA.0000000000000881

much attention to non-HDL-C/apoA-I and monocyte to high-density lipoprotein cholesterol ratio (MHR), which are more convinced for predicting the severity of coronary artery stenosis. This study aimed to analyze the relationship between non-HDL-C/apoA-I and MHR and the severity of CAD.

Patients and methods

Study population

A total of 1867 patients who underwent coronary angiography were enrolled in our study and were admitted into the Department of Cardiology, Zhongnan Hospital, Wuhan University, from March 2013 to June 2018. The diagnosis of coronary heart disease was based on the WHO criteria (in 1979) and combined with coronary angiography. Among them, 385 non-CAD hospitalized patients were selected as control group, 1482 patients diagnosed as CAD were divided into three subgroups according to the tertiles of their SYNTAX score: mild group, moderate group, and severe group.

Exclusion criteria various infectious diseases, hematopoietic diseases and severe anemia, surgery and severe trauma within 3 months, autoimmune diseases or those undergoing immunosuppressive therapy, malignant tumors, severe liver and kidney dysfunction, previous myocardial infarction, previous coronary artery stenting or coronary artery bypass grafting, cardiomyopathy, or decompensated heart failure. This study has been approved by the Medical Ethics Committee of our hospital.

Coronary angiography

Coronary angiography was performed by two experienced cardiologists in our hospital and the angiographic results were evaluated. Coronary angiography was performed according to the Judkin method through the radial or femoral approach. The degree of stenosis of the left main coronary artery, anterior descending artery, circumflex artery, and right coronary artery was evaluated.

SYNTAX score and group

According to the results of coronary angiography, the degree of CAD was scored using the SYNTAX scoring system. The SYNTAX Score is a unique tool to score complexity of coronary artery disease. The SYNTAX score was calculated using the SYNTAX scoring website (http://www.syntaxscore.com/). The scores were divided into three groups according to the tertiles of scores: mild group (<8), moderate group (8–15), and severe group (>15).

Laboratory measurements

In our hospital, blood samples were collected from the antecubital vein on the fasting morning (fasting for more than 10 hours). The biochemical analyzer was used to measure complete blood cell counts, HDL-C, and other biochemical indicators. Non-HDL-C equals total cholesterol minus HDL-C, non-HDL-C/apoA-I was calculated as the ratio of serum non-HDL-C level (mmol/l) to serum apoA-I level (mmol/l), MHR was calculated by dividing the monocyte count with HDL-C.

Statistical analysis

Statistical analyses were performed using the statistical package for the social sciences version 23.0 software program (IBM Corp, Armonk, New York, USA). The continuous variables were given as mean ± SD (if normal distribution) and medians (interquartile ranges) (if not normal distribution). The categorical variables were given as percentages. The χ^2 test was used to compare the categorical variables between the groups. The Kolmogorov–Smirnov test was used to assess whether the variables were normally distributed. The Student's *t*-test or Mann–Whitney *U*-test was used to compare the continuous variables between the groups according to whether they were normally distributed or not. Spearman's coefficient was calculated to describe correlation of parameters with SYNTAX score. To identify the independent predictors of CAD, univariate and multivariate logistic regression analyses were performed. The results were evaluated within a 95% confidence interval and at a significance level of P value < 0.05.

Results

Basic clinical characteristics of the study participants

Table 1 showed that the control group had lower percentage of diabetes, hypertension, males, and smokers. For CAD group, fasting blood glucose, serum creatinine, triglycerides, hypersensitive C-reactive protein, white blood cell count, monocyte count, lymphocyte count,

Table 1 Basic clinical characteristics of the study participants

Variables	Control group	CAD group	*P* value
Age	58.19 ± 10.70	63.10 ± 10.63	0.769
Gender [man (%)]	208 (54.0%)	1028 (83.4%)	0.000*
Smoking	94 (21.7%)	594 (40.1%)	0.015**
Diabetes	48 (12.5%)	448 (30.2%)	0.000*
Hypertension	314 (69.3%)	1017 (68.5%)	0.000*
FBG (mmol/l)	5.36 ± 1.20	7.36 ± 17.60	0.023**
Cr (mmol/l)	72.06 ± 18.40	78.58 ± 32.34	0.001*
UA (mmol/l)	333.61 ± 96.65	353.01 ± 101.42	0.957
TC (mmol/l)	4.50 ± 1.00	4.35 ± 1.33	0.189
TG (mmol/l)	1.71 ± 1.13	1.96 ± 1.72	0.008*
HDL (mmol/l)	1.18 ± 0.29	1.07 ± 0.27	0.170
LDL (mmol/l)	2.78 ± 0.88	2.71 ± 0.94	0.955
ApoA-I (mmol/l)	1.30 ± 0.24	1.17 ± 0.25	0.767
Non-HDL-C (mmol/l)	3.31 ± 0.99	2.62 ± 0.88	0.417
hs-CRP (mg/l)	3.10 ± 7.52	9.20 ± 21.20	0.000*
WBC (10^9/l)	6.34 ± 1.98	7.50 ± 3.14	0.000*
MONO (10^9/l)	0.45 ± 0.15	0.53 ± 0.23	0.000*
LYMP (10^9/l)	2.75 ± 0.67	1.66 ± 0.6	0.000*
MHR	0.40 ± 0.20	0.53 ± 0.30	0.000*
Non-HDL-C/apoA-I	2.62 ± 0.88	2.91 ± 1.17	0.036**

apoA-I, apolipoprotein A-I; CAD, coronary artery disease; Cr, creatinine; FBG, fasting blood glucose; HDL, high-density lipoprotein; hs-CRP, hypersensitive C-reactive protein; LDL, low-density lipoprotein; LYMP, lymphocyte count; MHR, monocyte/high-density lipoprotein cholesterol ratio; MONO, monocyte count; non-HDL-C, non–high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; UA, uric acid; WBC, white blood cell count.
*$P < 0.01$.
**$P < 0.05$.

Table 2 Clinical characteristics of three subgroups for patients with coronary artery disease

Variables	Mild (n = 445)	Moderate (n = 497)	Severe (n = 540)
Age	61.84 ± 11.00	63.00 ± 9.96*	64.40 ± 10.74***
Gender [man (%)]	277 (62.2%)	315 (63.3%)	396 (73.3%)***
Smoking	157 (35.2%)	187 (37.6%)	222 (41.1%)
Diabetes	110 (24.7%)	136 (27.3%)	185 (34.2%)*
Hypertension	290 (65.1%)	324 (65.2%)	371 (68.7%)
FBG (mmol/l)	7.22 ± 18.64	6.26 ± 2.21	8.58 ± 24.28
Cr (mmol/l)	76.35 ± 24.32	78.22 ± 36.48	80.03 ± 30.13
UA (mmol/l)	351.82 ± 101.80	344.71 ± 103.68	362.07 ± 100.01**
TC (mmol/l)	4.34 ± 1.79	4.35 ± 1.04	4.38 ± 1.18
TG (mmol/l)	1.89 ± 1.37	2.05 ± 1.95	1.94 ± 1.81
HDL (mmol/l)	1.10 ± 0.30	1.07 ± 0.26	1.05 ± 0.25*
LDL (mmol/l)	2.65 ± 0.92	2.69 ± 0.86	2.80 ± 1.02*
ApoA-I (mmol/l)	1.19 ± 0.24	1.19 ± 0.29	1.14 ± 0.23***
Non-HDL-C (mmol/l)	3.25 ± 1.78	3.28 ± 1.02	3.33 ± 1.34
hs-CRP(mg/l)	6.84 ± 17.57	7.25 ± 14.86	13.14 ± 28.74***
WBC (10^9/l)	7.24 ± 2.88	7.30 ± 2.53	7.91 ± 3.78***
MONO (10^9/l)	0.50 ± 0.20	0.52 ± 0.21	0.55 ± 0.25***
LYMP (10^9/l)	1.65 ± 0.60	1.68 ± 0.60	1.65 ± 0.69
MHR	0.50 ± 0.26	0.52 ± 0.21	0.56 ± 0.30***
Non-HDL/apoA-I	2.84 ± 1.46	2.88 ± 0.95	3.01 ± 1.10*

ApoA-I, apolipoprotein A-I; Cr, creatinine; FBG, fasting blood glucose; HDL, high-density lipoprotein; hs-CRP, hypersensitive C-reactive protein; LDL, low-density lipoprotein; LYMP, lymphocyte count; MHR, monocyte/high-density lipoprotein cholesterol ratio; MONO, monocyte count; non-HDL-C, non–high-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride; UA, uric acid; WBC, white blood cell count.
*$P < 0.05$ (compared with mild group).
**$P < 0.05$ (compared with moderate group).

Table 3 Multivariable logistic regression analysis of independent factors for coronary artery disease

Variables	B	Wald	*P* value	OR	95% CI
Age	0.053	46.600	<0.01	1.054	1.039–1.071
Smoking	0.610	10.461	<0.01	1.841	1.272–2.664
Diabetes	0.771	15.363	<0.01	2.163	1.471–3.181
Hypertension	0.408	7.238	0.007	1.504	1.117–2.026
hs-CRP	0.024	5.081	0.024	1.024	1.003–1.046
MHR	1.293	5.755	0.016	3.645	1.267–10.486
Non-HDL-C/apoA-I	0.740	14.828	<0.01	2.096	1.438–3.054

ApoA-I, apolipoprotein A-I; CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; hs-CRP, hypersensitive C-reactive protein; MHR, monocyte/high-density lipoprotein cholesterol ratio; OR, odds ratio.

non-HDL-C/apoA-I, and MHR were higher than those of the control group.

Basic clinical characteristics of coronary artery disease group and the level of non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio

The coronary heart disease group was divided into three groups according to the SYNTAX score tertile. The non-HDL-C/apoA-I and MHR levels were compared between the three groups. The results showed that non-HDL-C/apoA-I levels were higher compared with mild group ($P < 0.05$), and there was no significant difference between mild and moderate group, moderate and severe group. While the MHR level in severe group was higher than that in mild group and moderate group, there was no significant difference in MHR levels between moderate group and mild group ($P < 0.05$) (see in Table 2).

Relationships between non–high-density lipoprotein cholesterol/apolipoprotein A-I and monocyte/high-density lipoprotein cholesterol ratio and SYNTAX score

Spearman correlation analysis was performed on non-HDL-C/apoA-I and MHR with SYNTAX score. The results showed that non-HDL-C/apoA-I and MHR level was positively correlated with SYNTAX score ($r = 0.081$, $P < 0.001$; $r = 0.216$, $P < 0.001$, respectively).

Analysis of risk factors for coronary artery disease

To determine the independent predictors of CAD, we performed multivariable logistic regression analysis by using variables that showed statistically significant associations in the univariate regression analysis ($P < 0.05$). The results showed age, smoking, diabetes, hypertension, and hypersensitive C-reactive protein and MHR, non-HDL-C/apoA-I can be used as independent risk factors for CAD (see in Table 3).

Discussion

CAD has high incidence and mortality and has an effect on the quality of people's life. Atherosclerosis is a pathophysiological process involving multiple mechanisms, including oxidative stress, hypoxia, inflammation, vascular endothelial damage, platelet aggregation, etc. The activation of inflammatory cells and release of inflammatory factors play an important role in the process of formation, development, and rupture of atherosclerotic plaques. Activation of monocytes is an important step

in the initiation of inflammation, and it promotes the development of atherosclerosis [9]. During the process of development and deterioration of atherosclerosis, arterial vascular endothelium damage, circulating monocytes adhere to the vascular endothelium and penetrate into the blood vessel wall to form macrophages which phagocytose oxidized low-density lipoprotein (LDL) through scavenger receptors and turn into a foam cell [10]. Foam cells secrete proinflammatory cytokines, which could lead to vascular smooth muscle cell proliferation, migration, and plaque formation. In the process of the occurrence and development of atheroma, various cytokines act on hematopoietic tissues and stimulate the compensatory proliferation of monocytes, and causing the increase of peripheral blood mononuclear cells. Therefore, peripheral blood monocytes serve as a source of tissue macrophages and foam cells, their number reflects the progression of plaque and can be used to predict the progression of atherosclerosis [11].

Dyslipidemia is a major risk factor for CAD. HDL-C plays its role in antioxidation and prevents thrombosis by removing cholesterol from macrophages [12]. In addition, HDL-C also maintains endothelial function and low blood viscosity, it has antiatherosclerotic properties [13]. Studies have shown that HDL-C exhibits anti-inflammatory properties mainly by inhibiting monocyte activation by its major protein component apoA-I, which could reverse and inhibit LDL oxidation [14]. ApoA-I is the main component of HDL, it is mainly involved in the transportation of cholesterol and has an important role in immune regulation and inflammatory response [15]. Duong pointed out that apoA-I mediates intercellular cholesterol transportation mainly through ABCA1 on the membrane of cell [16]. In addition, ApoA-I activates lecithin cholesterol acyltransferase, resulting in the maturation of HDL particles [17]. Studies have shown that apoA-I can inhibit apoptosis of cell and platelet activation to exert antiatherosclerosis [18]. Therefore, studies have reported that a certain increase in serum HDL-C levels can improve atherosclerosis and reduce the risk of cardiovascular events [19]. Non-HDL-C is the sum of serum lipids excluding HDL-C. Many studies have shown that it has a key role in the occurrence of atherosclerotic cardiovascular disease events. A study shows that non-HDL-C is closely related to the asymptomatic intracranial arterial stenosis [20]. The study illustrated that the relationship between non-HDL-C levels and cardiovascular prognosis, the incidence of long-term major adverse cardiovascular event increased with increasing levels of non-HDL-C after acute myocardial infarction compared to attaining LDL-C target [21]. Therefore, we come to a conclusion that the non-HDL-C level is an important risk factor for the atherosclerotic cardiovascular disease [22]. Based on the mechanisms and roles of monocytes and HDL-C in atherosclerosis, MHR is an important indicator and predictor of CAD and cardiovascular events. Kanbay *et al.* [23] have shown that increased MHR is associated with adverse cardiovascular events and is an independent predictor of chronic kidney disease and major cardiovascular events. Karataş *et al.* [24] found that MHR was associated with major adverse cardiovascular events and mortality in patients with ST-segment elevation myocardial infarction, the major adverse cardiovascular events increased by 2.81 times and the risk of death increased by 19.15 times in the higher MHR group. Akboga *et al.* [25] found that for patients with stable angina, MHR is associated with the extent of coronary atherosclerosis and SYNTAX score. The higher the MHR is, the higher the SYNATX score is. Canpolat confirmed that elevated MHR levels may reflect increased levels of inflammation and oxidative stress, and MHR is closely related to the occurrence of slow coronary flow [26]. MHR was also found to be an independent predictor of recurrence after radiofrequency ablation of atrial fibrillation [27].

The SYNTAX score is an anatomical integral system based on coronary angiography for assessing the extent of CAD and the severity of artery stenosis. At present, there are fewer studies on the severity of MHR and CAD, and they are all small sample and single-center studies. In this study, the SYNTAX score was used to assess the severity of CAD. One thousand eight hundred sixty-seven patients with coronary angiography were included. The results showed a positive correlation between MHR and SYNTAX scores. It was found that the higher the MHR level, the higher the SYNTAX score, and the more severe the coronary stenosis. Multivariate logistic regression analysis showed that MHR was an independent risk factor for CAD. Our study also added non-HDL-C/apoA-I which serves as a biomarker for the extent of CAD. Our results showed that with the increase of non-HDL-C/apoA-I levels, the SYNTAX score increased, coronary stenosis is more severe. Multivariate logistic regression analysis showed that non-HDL-C/apoA-I was an independent risk factor for coronary heart disease as well. The use of non-HDL-C/apoA-I and MHR in clinical practice to assess the severity of CAD, which is easy, rapid, economical, and less affected by other indicators of inflammation, such as white blood cells and C-reactive protein.

In conclusion, non-HDL-C/apoA-I and MHR are easy to obtain biomarkers of inflammatory response, which are closely related to the severity of CAD and artery stenosis, they could be independent risk factors for CAD. The importance of non-HDL-C/apoA-I and MHR should be emphasized in clinical practice. Early detection can improve the diagnosis and prognosis of patients with CAD.

Conclusion

This study revealed that non-HDL-C/apoA-I and MHR have significant association with SYNTAX score and may be a potential available, easily measurable, and

inexpensive parameter for determining the coronary atherosclerosis severity. It may be a part of cardiovascular examination to identify individuals with CAD. However, to evaluate the predictive value of non-HDL-C/apoA-I and MHR, especially its prognostic value in patients with CAD, large-scale and prospective studies are still required.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (grant number 81670409).

Conflicts of interest

There are no conflicts of interest.

References

1 Libby P, Ridker PM, Hansson GK; Leducq Transatlantic Network on Atherothrombosis. Inflammation in atherosclerosis: from pathophysiology to practice. *J Am Coll Cardiol* 2009; **54**:2129–2138.
2 Kuhar MB. Executive summary of the third report of The National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). *JAMA* 2001; **106**:3143–3421.
3 Liu J, Sempos C, Donahue RP, Dorn J, Trevisan M, Grundy SM. Joint distribution of non-HDL and LDL cholesterol and coronary heart disease risk prediction among individuals with and without diabetes. *Diabetes Care* 2005; **28**:1916–1921.
4 Cui Y, Blumenthal RS, Flaws JA, Whiteman MK, Langenberg P, Bachorik PS, Bush TL. Non-high-density lipoprotein cholesterol level as a predictor of cardiovascular disease mortality. *Arch Intern Med* 2001; **161**:1413–1419.
5 Ossoli A, Pavanello C, Calabresi L. High-density lipoprotein, lecithin: cholesterol acyltransferase, and atherosclerosis. *Endocrinol Metab (Seoul)* 2016; **31**:223–229.
6 Rye KA, Barter PJ. Antiinflammatory actions of HDL: a new insight. *Arterioscler Thromb Vasc Biol* 2008; **28**:1890–1891.
7 Riwanto M, Landmesser U. High density lipoproteins and endothelial functions: mechanistic insights and alterations in cardiovascular disease. *J Lipid Res* 2013; **54**:3227–3243.
8 Groh L, Keating ST, Joosten LAB, Netea MG, Riksen NP. Monocyte and macrophage immunometabolism in atherosclerosis. *Semin Immunopathol* 2018; **40**:203–214.
9 Weber C, Shantsila E, Hristov M, Caligiuri G, Guzik T, Heine GH, *et al.* Role and analysis of monocyte subsets in cardiovascular disease. Joint consensus document of the European Society of Cardiology (ESC) working groups "atherosclerosis & vascular biology" and "thrombosis". *Thromb Haemost* 2016; **116**:626–637.
10 Jaipersad AS, Lip GY, Silverman S, Shantsila E. The role of monocytes in angiogenesis and atherosclerosis. *J Am Coll Cardiol* 2014; **63**:1–11.
11 Gratchev A, Sobenin I, Orekhov A, Kzhyshkowska J. Monocytes as a diagnostic marker of cardiovascular diseases. *Immunobiology* 2012; **217**:476–482.
12 Rosenson RS, Brewer HB Jr, Davidson WS, Fayad ZA, Fuster V, Goldstein J, *et al.* Cholesterol efflux and atheroprotection: advancing the concept of reverse cholesterol transport. *Circulation* 2012; **125**:1905–1919.
13 Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High density lipoprotein as a protective factor against coronary heart disease. The Framingham study. *Am J Med* 1977; **62**:707–714.
14 Murphy AJ, Westerterp M, Yvan-Charvet L, Tall AR. Anti-atherogenic mechanisms of high density lipoprotein: effects on myeloid cells. *Biochim Biophys Acta* 2012; **1821**:513–521.
15 Gordon SM, Hofmann S, Askew DS, Davidson WS. High density lipoprotein: it's not just about lipid transport anymore. *Trends Endocrinol Metab* 2011; **22**:9–15.
16 Duong PT, Weibel GL, Lund-Katz S, Rothblat GH, Phillips MC. Characterization and properties of pre beta-HDL particles formed by ABCA1-mediated cellular lipid efflux to apoa-I. *J Lipid Res* 2008; **49**:1006–1014.
17 Liang HQ, Rye KA, Barter PJ. Cycling of apolipoprotein A-I between lipid-associated and lipid-free pools. *Biochim Biophys Acta* 1995; **1257**:31–37.
18 Georgila K, Vyrla D, Drakos E. Apolipoprotein A-I (ApoA-I), immunity, inflammation and cancer. *Cancers (Basel)* 2019; **11**:1097.
19 Van de Woestijne AP, Van der Graaf Y, Liem AH, Cramer MJ, Westerink J, Visseren FL, *et al.* Low high-density lipoprotein cholesterol is not a risk factor for recurrent vascular events in patients with vascular disease on intensive lipid-lowering medication. *J Am Coll Cardiol* 2013; **62**:1834–1841.
20 Wu J, Wang A, Li X, Wu S, Zhao X. Non-high-density lipoprotein cholesterol levels on the risk of asymptomatic intracranial arterial stenosis: a result from the APAC study. *Sci Rep* 2016; **6**:37410.
21 Wongcharoen W, Sutthiwutthichai S, Gunaparn S, Phrommintikul A. Is non-HDL-cholesterol a better predictor of long-term outcome in patients after acute myocardial infarction compared to LDL-cholesterol?: a retrospective study. *BMC Cardiovasc Disord* 2017; **17**:10.
22 Holewijn S, den Heijer M, Swinkels DW, Stalenhoef AF, de Graaf J. non-HDL cholesterol and LDL cholesterol for identifying individuals at increased cardiovascular risk. *J Intern Med* 2010; **268**:567-77.
23 Kanbay M, Solak Y, Unal HU, Kurt YG, Gok M, Cetinkaya H, *et al.* Monocyte count/HDL cholesterol ratio and cardiovascular events in patients with chronic kidney disease. *Int Urol Nephrol* 2014; **46**:1619–1625.
24 Karataş MB, Çanga Y, Özcan KS, İpek G, Güngör B, Onuk T, *et al.* Monocyte to high-density lipoprotein ratio as a new prognostic marker in patients with STEMI undergoing primary percutaneous coronary intervention. *Am J Emerg Med* 2016; **34**:240–244.
25 Akboga MK, Balci KG, Maden O, Ertem AG, Kirbas O, Yayla C, *et al.* Usefulness of monocyte to HDL-cholesterol ratio to predict high SYNTAX score in patients with stable coronary artery disease. *Biomark Med* 2016; **10**:375–383.
26 Canpolat U, Çetin EH, Cetin S, Aydin S, Akboga MK, Yayla C, *et al.* Association of monocyte-to-HDL cholesterol ratio with slow coronary flow is linked to systemic inflammation. *Clin Appl Thromb Hemost* 2016; **22**:476–482.
27 Canpolat U, Aytemir K, Yorgun H, Şahiner L, Kaya EB, Çay S, *et al.* The role of preprocedural monocyte-to-high-density lipoprotein ratio in prediction of atrial fibrillation recurrence after cryoballoon-based catheter ablation. *Europace* 2015; **17**:1807–1815.