Cardiology and Cardiovascular Research
2025, Vol. 9, No. 1, pp. 25-31
https://doi.org/10.11648/j.ccr.20250901.12

Research Article

Correlation Between Serum Apolipoprotein A and Clinical Outcome in Patients with Non-ischemic Heart Failure

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Abstract

Previous studies on the correlation between serum apolipoprotein A-I (apoA-I) and the severity of heart failure (HF) as well as short-term clinical outcomes in patients with heart failure due to non-ischemic cardiomyopathy (NICM) have been inconclusive. To address this, we aimed to determine the impact of apoA-I on the severity of heart failure and short-term clinical outcomes in patients with HF due to NICM. In this single-center, observational study, we recruited 154 patients with NICM heart failure (NYHA functional class II-IV) and 80 control patients with normal cardiac function. Baseline characteristics were collected during hospitalization, and follow-up records were obtained 6 months after discharge. Statistical analyses included Pearson's chi-squared test and Spearman's correlation analysis, while the receiver operating characteristic (ROC) curve was used to discriminate patients with severe heart failure. Results showed that serum apoA-I levels were significantly lower in the heart failure group compared to controls and decreased with increasing cardiac function class. Additionally, serum apoA-I was positively correlated with left ventricular ejection fraction (LVEF) and negatively correlated with B-type natriuretic peptide (BNP) and cardiac function class. Patients who experienced clinical events within 6 months of discharge had significantly lower apoA-I concentrations compared to those without events. In conclusion, low serum apoA-I concentrations in patients with NICM and heart failure may be associated with more severe heart failure and a higher probability of recurrent clinical events in the short term.

Keywords

Heart Failure, Apolipoprotein A-I, Heart Rate, Cardiac Function, Clinical Outcome

1. Introduction

Heart failure (HF) is the final stage in the development of various cardiovascular diseases [1, 2]. It is a group of syndromes in which various structural and/or functional heart diseases lead to impaired ventricular filling and/or ejection function. In this stage, the cardiac output cannot meet the metabolic needs of body's tissues, with clinical manifestations of pulmonary and/or body circulation stasis and insufficient blood perfusion to organs and tissues [3-5]. HF has typical symptoms (e.g. shortness of breath, ankle edema and fatigue) and signs (increased jugular venous pressure, fine rales in the

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Received: 4 January 2025; **Accepted:** 22 January 2025; **Published:** 10 February 2025

lungs, displaced apical pulses). It is a worldwide health problem with a high morbidity and mortality rate and a trend towards younger population [6, 7]. Apolipoprotein A (apoA) is the major structural protein of high-density lipoprotein (HDL-C), of which apoA-I and apoA- II account for about 90% of the protein [8-10]. The ratio of apoA -I to apoA- II is about 3:1 [11]. Since apoA- I catalyzes lecithin-cholesterolacyltran sferase (LCAT) to transport excess cholesterol esters from tissues to the liver for disposal, apoA-I has tissue lipid scavenging and anti-atherosclerotic effects [12]. Therefore, apoA-I and apoB have also been used as risk factors to predict coronary heart disease [13, 14]. It has been demonstrated that low concentrations of serum apoA-I may affect the development and prognosis of coronary artery disease [15]. In patients with chronic heart failure, it has been found that low total serum cholesterol may be associated with poor prognosis. However, few studies have been conducted to assess the severity and prognosis of apoA-I in Chinese patients with chronic heart failure, especially those with non-ischemic heart failure. The aim of this study was to investigate the correlation between serum apoA-I concentrations and the severity as well as clinical outcome of heart failure patients with non-ischemic cardiomyopathy (NICM).

2. Methods

2.1. Study Population and Data Collection

Between July 2018 and July 2021, one hundred and fifty-four patients with chronic heart failure who were hospitalized in the Department of Cardiology, the First Hospital Affiliated to Soochow University were enrolled, and the diagnostic criteria were referred to the guidelines for the diagnosis and management of heart failure published by the European Society of Cardiology (ESC) in 2012 and graded according to the New York Heart Association (NYHA) cardiac function classification. Patients with ischemic cardiomyopathy, pulmonary embolism, myocarditis, autoimmune diseases, and primary diseases with severe pulmonary, hepatic, renal, hematologic, connective tissue, and neoplastic complications were excluded. All subjects were followed up to 6 months after hospital discharge until the first of the following clinical events occurred: all-cause death and rehospitalization due to heart failure exacerbation.

2.2. Clinical Assessment

All subjects were recorded age, sex, height, weight, calculated body mass index BMI (weight (kg) / height^2 (m^2)) and other general information. The history of hypertensive disease, diabetes mellitus, atrial fibrillation and smoking were also recorded. In each group, 5 ml of fasting elbow venous blood was collected in the early morning of the second day of admission and sent to the laboratory for the determination of glutamyl aminotransferase (ALT), glutamic aminotransferase (AST), creatinine (Cr), total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), apolipoprotein A (apo-A), and superoxide dismutase (hs-CRP). Sensitive C-reactive protein (hs-CRP) and other biochemical indexes were used to calculate creatinine clearance (CrCl) according to the Cockcroft-Gault formula, CrCl = (140-age) × body weight (Kg) / (0.818 × creatinine (umol/L)) in male patients; CrCl = (140-age) × body weight (Kg) × 0.85 / (0.818 ×creatinine (umol/L)). 3 ml of venous blood was collected and placed in anticoagulation tubes containing ethylenediaminetetraacetic acid (EDTA) and sent to the laboratory. B-type amino-terminal natriuretic peptidogen (BNP) was measured by electrochemiluminescence immunoassay on a Roche Elecsys E170 automatic immunoassay analyzer. The included patients underwent cardiac ultrasound (GE VIVIDi/VIVIq color echocardiograph, USA) in the cardiac ultrasound room on the second day after admission, and left ventricular ejection fraction (LVEF) was recorded. This cardiac echocardiography was conducted by an echocardiographer who was not involved in the study. The ethical approval for this study was obtained from the Ethics Committees of the First Affiliated Hospital of Soochow University. The ethics code for this study is SS2018072.

2.3. Statistical Analysis

All data were processed using SPSS 26.0 statistical software. The measurement data were expressed as mean ± standard deviation ($\bar{x}$±SD). One-way ANOVA followed by Bonferroni, Tukey, or Games-Howell post hoc test (dependent on the result of Levene's test to determine the equality of variances) was used to examine the effect of cardiac function. Pearson's correlation analysis and Spearman's correlation analysis were used for correlation analysis, while the results of individual tests were plotted as receiver operating characteristic curve (ROC), and the area under the curve (AUC) was calculated. A value of $p < 0.05$ (two-sided) was considered to be statistically significant.

3. Results

3.1. Comparison of Clinical Characteristics Between Control Group and NICM Heart Failure Patients with Cardiac Function Class II-IV (NYHA)

In total, 154 patients with chronic heart failure were enrolled, including 108 males and 46 females with a mean age of 63.79 ± 11.25 years. The control group consisted of 80 individuals with normal heart function, including 41 males and 39 females, with a mean age of 60.31 ± 8.75 years. The patients were divided into four groups (80 control, 18 class II, 49 class III, and 87 class IV) according to the NYHA classification of

heart failure severity, and the comparison between the groups is shown in Table 1. Clinical characteristics such as age, sex, BMI, incidence of diabetes, incidence of atrial fibrillation, smoking rate, systolic and diastolic blood pressure were not significantly different between the groups. There was no significant difference in the etiology of heart failure in the heart failure group, but with the increase of NYHA classification, the heart rate of patients gradually increased, and the difference of heart rate among the groups was statistically significant. The biochemical parameters of total cholesterol (TC), triglycerides (TG), low-density cholesterol (LDL-C), high-density cholesterol (HDL-C), apolipoprotein B (apoB), lipoprotein a (LP(a)), creatinine content (Cr), creatinine clearance (CrCl), and hypersensitive C-reactive protein (Hs-CRP) were not significantly different among the three groups in heart failure. However, the concentration of apolipoprotein A-I (apoA-I) decreased gradually with increasing NYHA classification ($p<0.05$). With increasing severity of heart failure, BNP gradually increased and LVEF values gradually decreased ($p<0.05$).

Table 1. *Comparison of characteristics in patients with heart failure of different cardiac function grades.*

	Cardiac Function Classification (NYHA)				
	control (N=80)	**Grade II (N=18)**	**Grade III (N=49)**	**Grade IV (N=87)**	***P* value**
Age	60.31±8.75	63.67±12.12	64.33±9.96	63.52±11.86	>0.05
Male (%)	41(51.25%)	10(55.56%)	34(69.39%)	64(73.56%)	>0.05
BMI	23.79±2.51	23.95±3.09	24.36±3.36	23.82±4.35	>0.05
Diabetes (%)	7(8.75%)	2(11.11%)	9(18.37%)	14(16.09%)	>0.05
AF (%)	3(3.75%)	2(11.11%)	18(36.73%)	28(32.18%)	>0.05
Smoking (%)	18(22.50%)	8(44.44%)	14(28.57%)	29(33.33%)	>0.05
SP (mmHg)	124.89±14.81	138.72±32.16	125.76±24.12	118.48±21.52	>0.05
DP (mmHg)	77.75±8.47	83.72±20.55	76.00±14.73	74.66±13.95	>0.05
HR (bpm)	73.63±10.67	76.56±13.29	79.61±24.48	85.45±19.67	<0.05
Etiology					
Dilated cardiomyopathy (%)		11 (61.11%)	22 (44.90%)	58 (66.67%)	
Hypertension (%)		4 (22.22%)	22 (44.90%)	17 (19.54%)	>0.05
Heart Valve (%)		3 (16.67%)	5 (10.20%)	12 (13.79%)	
TC (mmol/L)	4.42±0.73	4.23±0.75	3.85±1.22	3.72±1.03	>0.05
TG (mmol/L)	1.59±0.88	1.40±0.69	1.32±0.95	1.08±0.58	>0.05
LDL-C (mmol/L)	2.63±0.64	2.59±0.61	2.28±0.84	2.33±0.84	>0.05
HDL-C (mmol/L)	1.17±0.27	1.05±0.20	1.03±0.37	0.95±0.30	>0.05
ApoAI (g/L)	1.32±0.27	1.21±0.15	1.15±0.23	1.02±0.19	<0.05
ApoB (g/L)	0.89±0.19	0.88±0.17	0.85±0.22	0.84±0.28	>0.05
LP(a) (mg/L)	171.51±196.79	149.19±123.91	107.52±82.11	155.56±228.75	>0.05
ApoAI/ApoB	1.56±0.39	1.44±0.41	1.43±0.38	1.35±0.38	>0.05
Cr (umol/L)	63.38±13.25	81.35±17.35	85.55±28.32	96.22±39.43	>0.05
CrCl (ml/min)	97.26±22.58	75.75±23.98	71.57±30.58	69.74±31.15	>0.05
BNP (pg/ml)	50.12±30.99	1741.37±1509.41	3079.44±2626.87	7401.92±7671.88	<0.05
LVEF (%)	66.39±51.21	43.22±15.20	39.33±17.95	31.94±12.10	<0.05
HsCRP (mg/L)	1.78±2.07	4.73±3.92	4.93±4.90	6.19±5.15	>0.05

Table 1. BMI, Body Mass Index; AF, atrial fibrillation; SP, systolic pressure; DP, diastolic pressure; HR, heart rate; TC, serum total cholesterol; TG, serum triglycerides; LDL-C, serum low-density cholesterol; HDL-C, serum high-density cholesterol; LVEF, left ventricular ejection fraction; Cr, serum creatinine; CrCl, creatinine clearance; BNP, B-type amino-terminal natriuretic peptidogen; CRP, C-reactive protein.

3.2. Correlation Analysis of Serum apoA-I Concentration with LVEF Value, BNP, and Cardiac Function Classification

Pearson and Spearman correlation analyses showed a positive correlation between serum apo-A and LVEF values (r=0.470, p<0.001); a negative correlation with BNP (r=-0.382, p<0.001); and a negative correlation with NYHA classification (r=-0.598, p<0.001) (Figure 1-Figure 3).

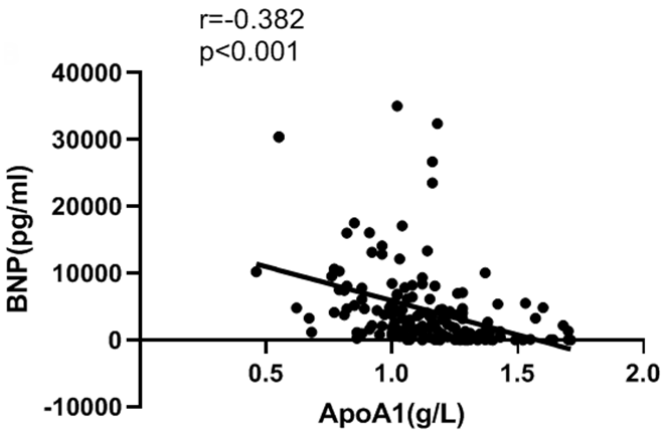

Figure 1. *Correlation analysis of serum apoA-I concentration with BNP.*

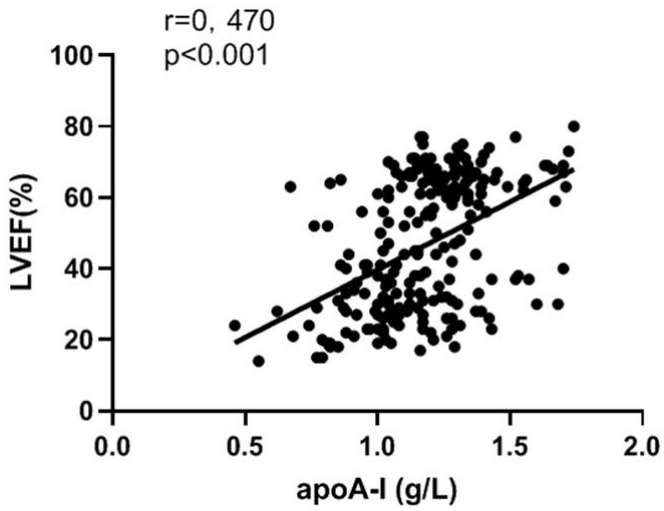

Figure 2. *Correlation analysis of serum apoA-I concentration with LVEF value.*

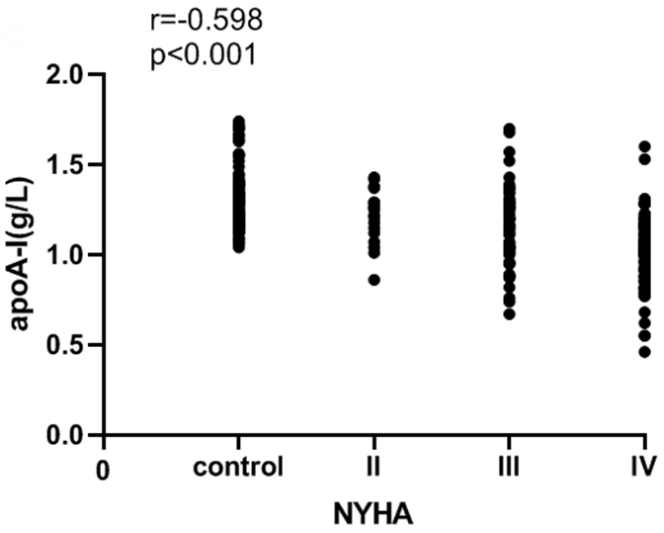

Figure 3. *Correlation analysis of serum apoA-I concentration with cardiac function classification.*

3.3. ROC Curve of Serum apoA-I Concentration to Evaluate the Severity of Heart Failure

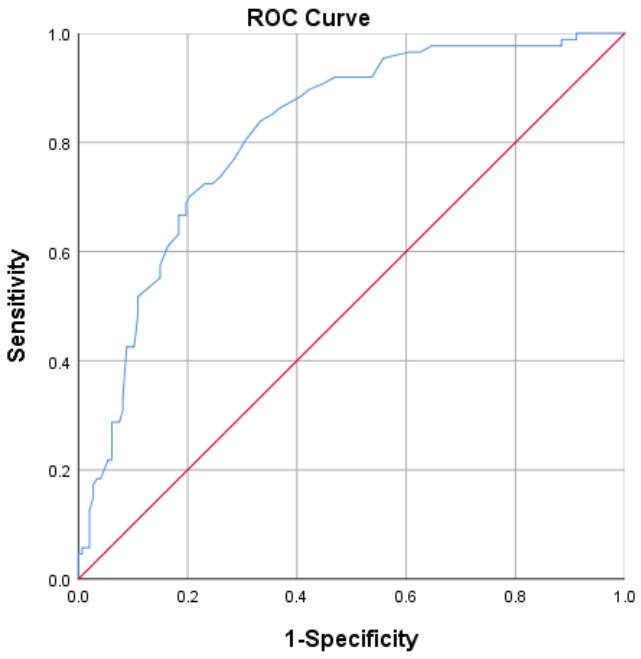

Figure 4. *ROC curve of serum apoA-I concentration to evaluate the severity of heart failure.*

According to NYHA classification, those with NYHA class IV were regarded as patients with severe heart failure, and the ROC curve was drawn to evaluate the reflection of apoA-I on the severity of chronic heart failure. The calculated AUC was 0.815, indicating that serum apoA-I concentration has a potential diagnostic value for the severity of clinical symptoms in patients with non-ischemic heart failure, and when apoA-I was 118.5 mg/dl, the sensitivity was 85.1% and the specificity

was 64.6% (see Figure 4).

3.4. Serum apoA-I Concentrations in Patients with Different Short-term Prognosis

At the follow-up within 6 months of discharge, 21 (13.63%) patients had a clinical event, 17 patients were readmitted for worsening heart failure symptoms, 3 patients died due to cardiac death, and 1 patient died from other causes (Table 2). apoA-I concentrations were statistically lower in patients in the group with clinical events compared with those in the group without clinical events (Figure 5, $p<0.05$).

Table 2. *Follow-up of patients with different cardiac function classifications at 6 months.*

	Grade II (N=18)	Grade III (N=49)	Grade IV (N=87)
Re-hospitalization due to worsening heart failure symptoms	1 (5.56%)	4 (8.16%)	12 (13.79%)
Death			
pump Failure	0 (0.00%)	0 (0.00%)	2 (2.30%)
sudden death	0 (0.00%)	0 (0.00%)	1 (1.15%)
other causes	0 (0.00%)	0 (0.00%)	1 (1.15%)

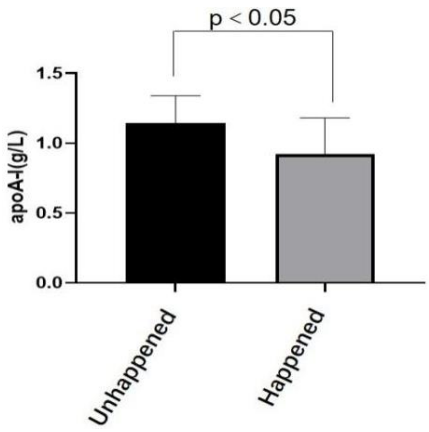

Figure 5. *Comparison of apoA-I levels in patients without and with clinical events.*

4. Discussion

High-density lipoprotein cholesterol (HDL-C) and its major protein component, apolipoprotein A-I (apoA-I), have been extensively studied for their roles in cardiovascular health and disease [16, 17]. Our study found that serum apoA-I levels were significantly lower in patients with non-ischemic cardiomyopathy (NICM) heart failure compared to controls, and these levels decreased further with increasing NYHA functional class. This observation is consistent with previous studies that have demonstrated a strong correlation between low apoA-I levels and poor prognosis in heart failure patients [18].

Several studies have investigated the role of apoA-I in both ischemic and non-ischemic heart failure. For example, apoA-I levels were significantly lower in patients with ischemic heart failure compared to non-ischemic heart failure, suggesting that the pathophysiological mechanisms underlying these two conditions may differ [19, 20]. Our findings in NICM patients align with these observations, highlighting the potential role of apoA-I in reflecting disease severity and prognosis.

The differences in apoA-I levels between ischemic and non-ischemic heart failure may be attributed to distinct underlying mechanisms. Ischemic heart failure is often associated with coronary artery disease, where atherosclerosis plays a significant role. ApoA-I, with its anti-inflammatory and anti-atherosclerotic properties, may be more directly involved in the pathogenesis of ischemic heart failure [21]. In contrast, non-ischemic cardiomyopathy may involve more diverse etiologies, such as genetic factors, infections, or autoimmune diseases, which may influence apoA-I levels differently [22].

Our study also examined the relationship between apoA-I and apoB levels. Previous research has shown that the apoA-I/apoB ratio can be a powerful predictor of cardiovascular risk [23, 24]. We found that while apoA-I levels were significantly associated with heart failure severity and clinical outcomes, apoB levels did not show similar correlations. This suggests that apoA-I may be a more sensitive biomarker for assessing disease progression in heart failure patients.

The significant correlation between apoA-I levels and heart failure severity highlights its potential as a biomarker for monitoring disease progression and predicting short-term outcomes [25]. Future studies should aim to validate these findings in larger cohorts and explore the role of apoA-I in different types of heart failure. Additionally, interventions targeting apoA-I, such as lifestyle modifications or pharmacological treatments, may be investigated to improve outcomes in heart failure patients [26]. The significant variation in heart rate between groups in our study reflects the body's

compensatory response to worsening cardiac function. This finding highlights the importance of considering heart rate as a clinical marker of heart failure severity and prognosis. In future studies, interventions aimed at managing heart rate (e.g., beta-blockers) may be further explored to improve outcomes in patients with advanced heart failure.

In conclusion, our study provides valuable insights into the role of apoA-I in non-ischemic heart failure. By comparing our findings with similar studies and discussing the potential mechanisms underlying the observed correlations, we hope to contribute to a better understanding of the pathophysiology of heart failure and the development of more effective diagnostic and therapeutic strategies.

Abbreviations

HF	Heart Failure
NICM	Non-ischemic Cardiomyopathy
NYHA	New York Heart Association
LVEF	Left Ventricular Ejection Fraction
BNP	B-type Natriuretic Peptide
HDL-C	High-Density Lipoprotein Cholesterol
apoA-I	Apolipoprotein A-I
apoB	Apolipoprotein B
LP(a)	Lipoprotein A
Cr	Creatinine
CrCl	Creatinine Clearance
Hs-CRP	Hypersensitive C-Reactive Protein
TC	Total Cholesterol
TG	Triglyceride
LDL-C	Low-Density Lipoprotein Cholesterol
ROC	Receiver Operating Characteristic
AUC	Area Under the Curve
ESC	European Society of Cardiology
LCAT	Lecithin-Cholesterol Acyltransferase
AF	Atrial Fibrillation
SP	Systolic Pressure
DP	Diastolic Pressure
HR	Heart Rate

Author Contributions

Chiqian Ma: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Writing – original draft

Licong Chen: Data curation, Investigation, Methodology, Software

Shikun Sun: Project administration, Resources

Xiaodong Qian: Resources, Validation

Yiren Qin: Conceptualization, Supervision, Writing – original draft, Writing – review & editing

Ethics Approval

The Ethics Committees of the First Affiliated Hospital of Soochow University approved this study. The participants provided their written informed consent to participate in this study.

Funding

This work was supported by the Suzhou Science and Technology Projects under grant SS202072, SKY2021065.

Data Availability Statement

Data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

[1] Petrie MC, Verma S, Docherty KF, Inzucchi SE, Anand I, Belohlavek J, Bohm M, Chiang CE, Chopra VK, de Boer RA *et al*: Effect of Dapagliflozin on Worsening Heart Failure and Cardiovascular Death in Patients With Heart Failure With and Without Diabetes. *JAMA* 2020, 323(14): 1353-1368. https://doi.org/10.1001/jama.2020.1906

[2] Yin J, Lu X, Qian Z, Xu W, Zhou X: New insights into the pathogenesis and treatment of sarcopenia in chronic heart failure. *Theranostics* 2019, 9(14): 4019-4029. https://doi.org/10.7150/thno.33000 eCollection 2019.

[3] Pinsky MR: The right ventricle: interaction with the pulmonary circulation. *Crit Care* 2016, 20: 266. https://doi.org/10.1186/s13054-016-1440-0

[4] Kraigher-Krainer E, Shah AM, Gupta DK, Santos A, Claggett B, Pieske B, Zile MR, Voors AA, Lefkowitz MP, Packer M *et al*: Impaired systolic function by strain imaging in heart failure with preserved ejection fraction. *J Am Coll Cardiol* 2014, 63(5): 447-456. https://doi.org/10.1016/j.jacc.2013.09.052

[5] Aaron CP, Hoffman EA, Lima JAC, Kawut SM, Bertoni AG, Vogel-Claussen J, Habibi M, Hueper K, Jacobs DR, Jr., Kalhan R *et al*: Pulmonary vascular volume, impaired left ventricular filling and dyspnea: The MESA Lung Study. *PLoS One* 2017, 12(4): e0176180. https://doi.org/10.1371/journal.pone.0176180 eCollection 2017.

[6] Liu L, Eisen HJ: Epidemiology of heart failure and scope of the problem. *Cardiol Clin* 2014, 32(1): 1-8, vii. https://doi.org/10.1016/j.ccl.2013.09.009

[7] Wong CM, Hawkins NM, Petrie MC, Jhund PS, Gardner RS, Ariti CA, Poppe KK, Earle N, Whalley GA, Squire IB *et al*: Heart failure in younger patients: the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC). *Eur Heart J* 2014, 35(39): 2714-2721. https://doi.org/10.1093/eurheartj/ehu216

[8] Segrest JP, Li L, Anantharamaiah GM, Harvey SC, Liadaki KN, Zannis V: Structure and function of apolipoprotein A-I and high-density lipoprotein. *Curr Opin Lipidol* 2000, 11(2): 105-115. https://doi.org/10.1097/00041433-200004000-00002

[9] Melchior JT, Street SE, Vaisar T, Hart R, Jerome J, Kuklenyik Z, Clouet-Foraison N, Thornock C, Bedi S, Shah AS *et al*: Apolipoprotein A-I modulates HDL particle size in the absence of apolipoprotein A-II. *J Lipid Res* 2021, 62: 100099. https://doi.org/10.1016/j.jlr.2021.100099

[10] De Oliveira e Silva ER, Kong M, Han Z, Starr C, Kass EM, Juo SH, Foster D, Dansky HM, Merkel M, Cundey K *et al*: Metabolic and genetic determinants of HDL metabolism and hepatic lipase activity in normolipidemic females. *J Lipid Res* 1999, 40(7): 1211-1221. https://doi.org/10.1016/S0022-2275(20)33483-0

[11] Pussinen PJ, Jauhiainen M, Ehnholm C: ApoA-II/apoA-I molar ratio in the HDL particle influences phospholipid transfer protein-mediated HDL interconversion. *J Lipid Res* 1997, 38(1): 12-21. https://doi.org/10.1016/S0022-2275(20)37271-0

[12] Millar JS, Cuchel M: ApoA-I-Directed Therapies for the Management of Atherosclerosis. *Curr Atheroscler Rep* 2015, 17(10): 60. https://doi.org/10.1007/s11883-015-0539-0

[13] Walldius G, Jungner I, Aastveit AH, Holme I, Furberg CD, Sniderman AD: The apoB/apoA-I ratio is better than the cholesterol ratios to estimate the balance between plasma proatherogenic and antiatherogenic lipoproteins and to predict coronary risk. *Clin Chem Lab Med* 2004, 42(12): 1355-1363. https://doi.org/10.1515/CCLM.2004.254

[14] Fernandez ML, Webb D: The LDL to HDL cholesterol ratio as a valuable tool to evaluate coronary heart disease risk. *J Am Coll Nutr* 2008, 27(1): 1-5. https://doi.org/10.1080/07315724.2008.10719668

[15] Srinivasan SR, Berenson GS: Serum apolipoproteins A-I and B as markers of coronary artery disease risk in early life: the Bogalusa Heart Study. *Clin Chem* 1995, 41(1): 159-164. https://doi.org/10.1016/S0140-6736(01)07098-2

[16] Rubenfire M, Brook RD: HDL cholesterol and cardiovascular outcomes: what is the evidence? *Curr Cardiol Rep* 2013, 15(4): 349. https://doi.org/10.1007/s11886-013-0349-3

[17] Barter P: HDL-C: role as a risk modifier. *Atheroscler Suppl* 2011, 12(3): 267-270. https://doi.org/10.1016/S1567-5688(11)70885-6

[18] Van Lenten BJ, Hama SY, de Beer FC, Stafforini DM, McIntyre TM, Prescott SM, La Du BN, Fogelman AM, Navab M: Anti-inflammatory HDL becomes pro-inflammatory during the acute phase response. Loss of protective effect of HDL against LDL oxidation in aortic wall cell cocultures. *J Clin Invest* 1995, 96(6): 2758-2767. https://doi.org/10.1172/JCI118345

[19] Zhang Y, Zanotti I, Reilly MP, Glick JM, Rothblat GH, Rader DJ: Overexpression of apolipoprotein A-I promotes reverse transport of cholesterol from macrophages to feces in vivo. *Circulation* 2003, 108(6): 661-663. https://doi.org/10.1161/01.CIR.0000086981.09834.E0

[20] Georgila K, Vyrla D, Drakos E: Apolipoprotein A-I (ApoA-I), Immunity, Inflammation and Cancer. *Cancers (Basel)* 2019, 11(8). https://doi.org/10.3390/cancers11081097

[21] Chiesa G, Sirtori CR: Recombinant apolipoprotein A-I (Milano): a novel agent for the induction of regression of atherosclerotic plaques. *Ann Med* 2003, 35(4): 267-273. https://doi.org/10.1080/07853890310005281

[22] Karjalainen MK, Holmes MV, Wang Q, Anufrieva O, Kahonen M, Lehtimaki T, Havulinna AS, Kristiansson K, Salomaa V, Perola M *et al*: Apolipoprotein A-I concentrations and risk of coronary artery disease: A Mendelian randomization study. *Atherosclerosis* 2020, 299: 56-63. https://doi.org/10.1016/j.atherosclerosis.2020.02.002

[23] Banos-Gonzalez MA, Pena-Duque MA, Angles-Cano E, Martinez-Rios MA, Bahena A, Valente-Acosta B, Cardoso-Saldana G, Angulo-Ortiz J, de la Pena-Diaz A: Apo(a) phenotyping and long-term prognosis for coronary artery disease. *Clin Biochem* 2010, 43(7-8): 640-644. https://doi.org/10.1016/j.clinbiochem.2010.01.013

[24] Sun L, Guo M, Xu C, Qiao X, Hua Y, Tuerhongjiang G, Lou B, Li R, Bai X, Zhou J *et al*: HDL-C/apoA-I Ratio Is Associated with the Severity of Coronary Artery Stenosis in Diabetic Patients with Acute Coronary Syndrome. *Dis Markers* 2021, 2021: 6689056. https://doi.org/10.1155/2021/6689056 eCollection 2021.

[25] Voigt A, Rahnefeld A, Kloetzel PM, Kruger E: Cytokine-induced oxidative stress in cardiac inflammation and heart failure-how the ubiquitin proteasome system targets this vicious cycle. *Front Physiol* 2013, 4: 42. https://doi.org/10.3389/fphys.2013.00042 eCollection 2013.

[26] Ayoub KF, Pothineni NVK, Rutland J, Ding Z, Mehta JL: Immunity, Inflammation, and Oxidative Stress in Heart Failure: Emerging Molecular Targets. *Cardiovasc Drugs Ther* 2017, 31(5-6): 593-608. https://doi.org/10.1007/s10557-017-6752-z