

Association between lipid profiles and arterial stiffness: A secondary analysis based on a cross-sectional study

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Abstract

Objectives: The relationship between lipid levels and arterial stiffness remains controversial. Therefore, we aimed to determine the relationship between lipid profiles and brachial–ankle pulse wave velocity (baPWV) as an indicator of arterial stiffness.

Methods: A total of 909 participants aged 24 to 84 years were stratified into four baPWV quartiles in our study. Serum lipids, baPWV, and other variables of the participants were measured. Univariable and multivariable linear regression analyses were used to examine the relationships between lipid parameters and baPWV.

Results: The highest baPWV quartile group had higher aspartate transaminase, alanine aminotransferase, plasma glucose, total cholesterol, triglyceride (TG), and low-density lipoprotein cholesterol levels and maximum ankle–brachial index, and lower high-density lipoprotein cholesterol levels and estimated glomerular filtration rate. Univariate regression analysis showed that total cholesterol, TG, and low-density lipoprotein cholesterol levels were positively related and high-

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density lipoprotein cholesterol levels were negatively related to baPWV. After adjusting for age, body mass index, smoking status, aspartate transaminase, alanine aminotransferase, plasma glucose, and estimated glomerular filtration rate, only TG levels were correlated with baPWV ($\beta = 0.075$).

Conclusions: Four lipid variates are associated with arterial stiffness, and TG levels are positively related to arterial stiffness, independent of cardiovascular risks and liver function.

Keywords

Arterial stiffness, lipid profile, brachial–ankle pulse-wave velocity, triglycerides, plasma glucose, estimated glomerular filtration rate

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Introduction

Arterial stiffness is due to structural and functional changes within the arterial walls, and it can be noninvasively measured as brachial–ankle pulse-wave velocity (baPWV). Arterial stiffening increases vascular damage and cardiovascular morbidity.¹ Increased baPWV is a significant predictor of cardiovascular events.² Dyslipidemia is an established risk factor in development and progression of cardiovascular disease (CVD)³ and the serum lipid profile has emerged as an independent predictor of CVD.⁴ Additionally, several epidemiological studies have reported that a high triglyceride (TG)/high-density lipoprotein cholesterol (HDL) ratio is positively associated with arterial stiffness in adolescent and adult populations.^{5,6} However, the relationship between baPWV and other lipids, including total cholesterol (TC) and low-density lipoprotein cholesterol (LDL), is unclear. Zhao et al.⁷ showed that only HDL was associated with a high baPWV, while Yiming et al.⁸ reported that only TG levels were significantly related to baPWV. Even though a large cross-sectional analysis showed that all lipid variables were

obviously correlated with baPWV, the participants were all Chinese patients with hypertension.⁹

In our study, we aimed to investigate the association between four lipid variables and arterial stiffness in the general healthy Japanese population by constructing multi-variable regression models.

Methods

Study population

All subjects in this study participated in a medical health check-up program that was conducted in the Medical Health Checkup Center at Murakami Memorial Hospital in Japan.¹⁰ The data were publicly available in the Dryad database.¹¹ Briefly, all individuals received measurements of baPWV at Murakami Memorial Hospital between March 2004 and December 2012. The study protocol was approved by the ethics review committee of Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine. The study was conducted in accordance with the Declaration of Helsinki with informed consent obtained from all participants. Details

regarding the aims and inclusion criteria of the trial have been described previously.^{10,12}

Data collection

A standardized physical examination and medical history were carried out for all participants. Body mass index (BMI) was calculated as the weight (kg) divided by the squared height (m²). Lifestyle factors, such as smoking status (current smoker) and regular exercise (at least once a week), were recorded by standardized questionnaires. We excluded alcohol consumption in the original data because of many missing records and four additional participants did not have regular exercise records.

Biochemical indices, including aspartate transaminase (AST), alanine aminotransferase (ALT), γ -glutamyltranspeptidase (γ GTP), uric acid, and fasting plasma glucose (FBG) levels, as well as lipids, including TC, TG, HDL, and LDL levels, were examined with MODULAR ANALYTISC (Hitachi High-Technologies Corp. Ltd., Tokyo, Japan).

The diagnosis of fatty liver was based on the results of abdominal ultrasonography (Aloka SSD-650CL; Aloka Co., Ltd., Tokyo, Japan). The estimated glomerular filtration rate (eGFR) was calculated using the Japanese Society of Nephrology equation.

BaPWV and the maximum ankle-brachial index (ABI_{max}) were measured with an automatic waveform analyzer (Colin Medical Technology, Komaki, Japan) by a previously reported method.¹³

Statistical analysis

Continuous variables are expressed as mean \pm standard deviation and categorical variables are expressed as numbers (percentages). The participants were stratified by quartiles of baPWV. Four groups of participants were compared by using the

ANOVA test. The relationships of lipid profiles and baPWV were examined by univariate linear regression analysis, as well as by multivariable linear regression analysis after adjusting for covariates as follows: model 1, adjusted for age, BMI, and smoking status; and model 2, with additional adjustment for biochemical data, including FPG, AST, ALT, and eGFR. All analyses were performed using SPSS software version 23 (IBM Corp., Armonk, NY, USA) and a two-tailed $P < 0.05$ was considered significant.

Results

Baseline characteristics of the study participants

A total of 909 participants aged 24 to 84 years were analyzed, and 590 were men. Of all participants, 21.7% were current smokers, 19.9% had regular exercise, and 18.9% were diagnosed with fatty liver. We further assigned participants into subgroups using baPWV quartiles (Q1: <12.7 m/s; Q2: 12.7–13.6 m/s; Q3: 13.7–15.1 m/s; Q4: ≥ 15.2 m/s). We found that patients had significantly higher systolic blood pressure and diastolic blood pressure (both $P < 0.001$), higher levels of AST, ALT, FBG, TC, TG, and LDL (all $P < 0.01$), and a higher ABI_{max} ($P < 0.001$) in the highest baPWV quartile. Patients also had a significantly lower eGFR in the highest baPWV quartile ($P < 0.001$) (Table 1).

Relation between lipid levels and baPWV

TC, TG, and LDL levels were significantly positively associated with baPWV, and HDL was negatively associated with baPWV (all $P < 0.05$) (Table 2 and Figure 1). Because cardiovascular risk can affect arterial stiffness, we added covariates, including age, BMI, and smoking status, to

Table 1. Clinical and laboratory characteristics of the study participants.

	Q1	Q2	Q3	Q4	P value
n (%)	226 (24.9)	226 (24.9)	227 (25.0)	230 (25.3)	
Male sex (n, %)	123 (54.4)	154 (68.1)	157 (69.2)	156 (67.8)	0.002
Age (years)	45.69 ± 8.91	48.93 ± 8.66	52.16 ± 8.23	57.64 ± 8.22	<0.001
BMI (kg/m ²)	22.61 ± 3.40	23.25 ± 3.34	23.33 ± 2.82	23.30 ± 2.87	0.042
SBP (mm Hg)	110.25 ± 11.01	117.34 ± 12.17	122.49 ± 12.84	130.59 ± 15.37	<0.001
DBP (mm Hg)	69.60 ± 7.67	74.45 ± 8.03	77.76 ± 9.08	82.54 ± 10.11	<0.001
Smoking (n, %)	51 (22.6)	47 (20.8)	56 (24.7)	43 (18.7)	0.456
Regular exercise (n, %)	46 (20.6)	42 (18.8)	42 (18.8)	48 (21.4)	0.856
Fatty liver (n, %)	33 (14.6)	67 (29.6)	75 (33.0)	88 (38.3)	<0.001
AST (IU/L)	19.02 ± 6.17	21.51 ± 10.22	20.70 ± 6.58	22.10 ± 8.43	<0.001
ALT (IU/L)	19.31 ± 12.28	24.15 ± 17.93	22.97 ± 11.91	24.19 ± 13.72	<0.001
γGTP (IU/L)	19.36 ± 18.64	25.08 ± 22.04	28.64 ± 31.77	28.47 ± 22.22	<0.001
FBG (mmol/L)	5.2 ± 0.5	5.4 ± 0.6	5.4 ± 0.6	5.7 ± 1.1	<0.001
Uric acid (μmol/L)	293.2 ± 83.9	313.5 ± 80.9	323.0 ± 85.7	320.0 ± 73.8	<0.001
TC (mmol/L)	5.20 ± 0.89	5.47 ± 0.89	5.46 ± 0.95	5.60 ± 0.94	<0.001
TG (mmol/L)	0.89 ± 0.62	1.15 ± 1.03	1.19 ± 0.79	1.28 ± 0.85	<0.001
HDL (mmol/L)	1.43 ± 0.37	1.39 ± 0.36	1.36 ± 0.36	1.36 ± 0.41	0.225
LDL (mmol/L)	3.16 ± 0.77	3.32 ± 0.78	0.75 ± 0.84	3.42 ± 0.87	0.005
eGFR (mL/minute/1.73 m ²)	74.55 ± 13.17	72.33 ± 11.37	69.27 ± 10.83	66.57 ± 10.82	<0.001
ABImax	1.18 ± 0.07	1.19 ± 0.07	1.20 ± 0.08	1.21 ± 0.13	<0.001

Q: quartile; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; AST: aspartate transaminase; ALT: alanine aminotransferase; γGTP: γ-glutamyltranspeptidase; FBG: fasting plasma glucose; TC: total cholesterol; TG: triglyceride; HDL: high-density lipoprotein; LDL: low-density lipoprotein; eGFR: estimated glomerular filtration rate; ABImax: maximum ankle-brachial index.

Table 2. Association between brachial-ankle pulse wave velocity and lipid parameters.

	Unadjusted		Adjusted model 1		Adjusted model 2	
	β (95% CI)	P	β (95% CI)	P	β (95% CI)	P
TC	0.104 (0.039–0.169)	0.002	0.025 (–0.031–0.082)	0.378	–0.011 (–0.067–0.045)	0.703
TG	0.134 (0.070–0.199)	<0.001	0.121 (0.063–0.179)	<0.001	0.075 (0.016–0.134)	0.012
HDL	–0.078 (–0.143–0.013)	0.018	–0.086 (–0.146–0.027)	0.005	–0.050 (–0.110–0.010)	0.101
LDL	0.084 (0.019–0.149)	0.011	0.025 (–0.032–0.082)	0.389	–0.012 (–0.069–0.045)	0.677

1. Adjusted for age, body mass index, and smoking status.

2. Adjusted for age, body mass index, smoking status, fasting plasma glucose, aspartate transaminase, alanine aminotransferase, and the estimated glomerular filtration rate.

CI, confidence interval; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

the multivariable linear regression model 1. Taking into consideration that liver function is a novel predictor of cardiovascular disease,¹⁴ we also included additional variables, such as AST and ALT, to model 2. After age, BMI, and smoking status were adjusted, the significance of the relationships between TC

and LDL with baPWV disappeared. The correlation of TG with baPWV still existed after adjustment for age, BMI, and smoking status (model 1, $P < 0.001$), and after adjustment for additional FPG, AST, ALT, and eGFR (model 2, $P = 0.012$). After adjustment for age, BMI and smoking status, HDL levels

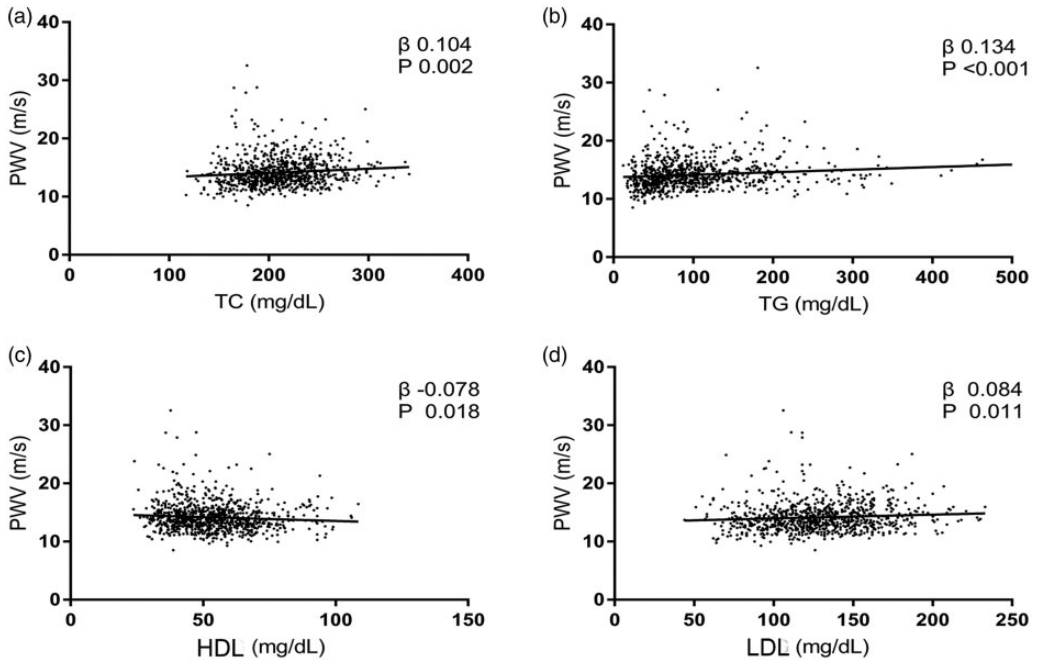


Figure 1. Associations between baPWV, as an indicator of arterial stiffness, and the lipid profile. Analysis was performed using a univariate linear regression model. The adjusted correlation coefficients were 0.104 for TC (a), 0.134 for TG (b), -0.078 for HDL (c), and 0.084 for LDL (d) levels. HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglyceride; PWV, pulse wave velocity.

were still negatively correlated with baPWV ($P = 0.005$).

Discussion

In this cross-sectional study, we showed a relationship between lipid profiles and baPWV in the general population. We found the following results. (1) TG, TC, and LDL levels were positively associated with baPWV. (2) HDL levels were negatively related to baPWV. (3) TG levels were positively associated with baPWV, even after adjustment for age, BMI, smoking status, FBG, AST, ALT, and eGFR. Therefore, TGs may be a surrogate lipid marker of arterial stiffness.

Our findings are consistent with the results of previous studies, which showed that a high TG/HDL ratio was positively

associated with arterial stiffness in the healthy adult population,⁵ adolescents, and young adults.⁶ We also found that TG levels were closely related to arterial stiffness in the general population, independent of age, BMI, smoking status, FBG, AST, ALT, and eGFR, while HDL levels were not correlated with arterial stiffness after adjustment for common cardiovascular risks and biochemical indices. Furthermore, a previous study called the China Stroke Primary Prevention Trial (CSPPT) showed that there was an association between the lipid profile and arterial stiffness in Chinese rural-dwelling adults with primary hypertension. In accordance with the CSPPT, we found that TC and LDL levels were positively associated with arterial stiffness and HDL levels were negatively related to arterial stiffness, but this

significance disappeared after adjustment for common cardiovascular risks and biochemical indices. This discrepancy between studies may be due to covariate adjustment because we adjusted for additional liver function in our model and our participants were healthy individuals.

Arterial stiffness results from structural and functional changes of the arterial walls. Some plausible mechanisms underlying the significant association between the lipid profile and baPWV are as follows. First, excess lipid and cholesterol can bind to the arterial intima and accumulate in the arterial wall, subsequently leading to arterial stiffness.¹⁵ Additionally, oxidative and nitrosative stress caused by excess lipids accelerates arterial stiffness.¹⁶ Finally, lipid and arterial stiffness may be associated with chronic inflammation in the vessel wall. Leukocytes stimulated by lipids release a variety of cytokines and adhesive molecules, which in turn leads to leukocytes adhering to vascular endothelium and penetrating the intima, resulting in increased vascular resistance.¹⁷

The following limitations should be considered in interpretation of this study. Our cross-sectional study showed correlations between lipid profiles and PaPWV, but we cannot conclude that lipids are a risk factor involved in the development of arterial stiffness. Second, the participants were all Japanese. Therefore, this relationship may not be applicable to other biogeographic ethnic groups. Third, self-reported of life-style data, including smoking status and regular exercise, may have been arbitrary and incomplete.

Conclusion

The present study shows that lipid parameters are correlated with arterial stiffness. HDL levels are inversely associated with baPWV after adjustment for cardiovascular risks, and TG levels are positively related to

baPWV independent of cardiovascular risks and liver function. Lipid-lowering therapy should be considered in the general healthy population at risk of arterial stiffness.

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Authors' contributions

YL designed the study; LW and JN wrote the first draft of the manuscript.

Availability of data and materials

Data can be downloaded from the DATADRYAD database (www.DataDryad.org).


Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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