# Discordance Between Apolipoprotein B or Non-HDL-Cholesterol and LDL-Cholesterol in Middle-aged and Elderly Chinese Patients Predicts Arterial Stiffness

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**Research Article**

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# Abstract

***Background:*** Discordance of lipid parameters is closely associated with residual cardiovascular risk. This study investigated the discordance between non-high-density lipoprotein cholesterol (non-HDL-C), or apolipoprotein B (apoB), and low-density lipoprotein cholesterol (LDL-C) and assessed arterial stiffness risk.

***Methods:*** This study included a total of 402 middle-aged and elderly Northern Chinese individuals, whose brachial-ankle pulse wave conduction velocity(baPWV), as well as clinical and biochemical data, were measured. Arterial stiffness was defined as the upper quartile of the baPWV. All participants were divided into four mutually exclusive concordance/discordance groups based on the lipid goal for very high-risk populations, according to the 2016 European Society of Cardiology / European Atherosclerosis Society guidelines. Discordance was defined as an LDL-C≥ 1.81mmol/L with non-HDL-C< 2.59mmol/L, or apoB <0.80mmol/L, or vice versa.

***Results:*** The mean age of the participants was 65.9±13.0 years, and 59.5% were male. The mean LDL-C was 2.41±0.81mmol/L, non-HDL-C 3.06±0.94mmol/L, and apoB 0.84±0.21mmol/L. LDL-C was observed to be discordant with non-HDL-C (20.1%) and apoB (30.8%). When stratified according to LDL-C levels, the baPWV was greater in those patients with higher non-HDL-C or apoB levels. The Spearman analysis showed a significant association between discordant lipid patterns and the presence of arterial stiffness(r= 0.131 and r=0.117, respectively). In the adjusted logistic regression model, low LDL-C and high non-HDL-C or apoB discordance were also associated with the risk of arterial stiffness (OR: 13.412 and OR: 13.054, respectively).

***Conclusions:*** There was discordance between the LDL-C and non-HDL-C, or apoB in middle-aged and elderly Chinese individuals, which was associated with a higher risk of arterial stiffness. The non-HDL-C or apoB levels could be used to identify individuals who could benefit from more intensive lipid modification.


# Background

Hyperlipidemia is associated with a higher risk of cardiovascular disease (CVD). Cholesterol control is easily achievable and presents a central aspect of atherosclerotic CVD prevention. Atherosclerotic CVD is linearly associated with low-density lipoprotein cholesterol (LDL-C); therefore, targeting LDL-C is recommended as a strategy in curtailing cardiovascular risk. However, many individuals, even those with optimal LDL-C levels, experience cardiovascular events or atherosclerosis progression. This phenomenon has been termed as the "residual risk"[1], which cannot be identified by measuring LDL-C. In addition, exclusive targeting of LDL-C is limited by measurement variability. Thus, increasing interest has been focused on the use of alternative lipid parameters. Many studies have shown that in addition to LDL-C, other lipid parameters, such as non-high-density lipoprotein cholesterol (non-HDL-C) or apolipoprotein B (apoB), can also increase the risk of CVD, which is conducive to the assessment and treatment of residual

risk because the major contributing risk factor for residual risk is the difference between the estimated LDL-C value and the actual quantity of circulating atherogenic lipoprotein particles. Non-HDL-C comprises cholesterol carried by all potentially atherogenic lipoprotein particles, including LDL-C, intermediate-density lipoproteins (IDL), very-low-density lipoproteins, remnant lipoproteins, and lipoprotein a (LPa). ApoB represents the number of atherogenic lipoprotein particles mentioned above because each lipoprotein particle contains one molecule of apoB [2]. LDL-C represents the total cholesterol concentration of LDL, IDL, and LPa particles. Cholesterol content within atherogenic lipoprotein particles varies substantially in approximately 10–20% of individuals, and the particles are either enriched or alternatively depleted in cholesterol [3]. When the atherogenic lipoprotein particle concentration within a standardized amount of cholesterol is consistent, the cholesterol concentration is considered to be concordant with the number of lipoprotein particles. Then, the cardiovascular risk can be accurately predicted by LDL-C, non-HDL-C, and apoB. However, when the cholesterol content is higher or lower than the average concentration, the cholesterol concentration is discordant with the number of lipoprotein particles, as is the cardiovascular risk predicted by LDL-C, non-HDL-C, and apoB. Several previous studies have investigated the discordance between LDL-C and non-HDL-C, or apoB [3–5]. The 2016 European Society of Cardiology / European Atherosclerosis Society (ESC / EAS) guidelines for the management of dyslipidemia advocate that non-HDL-C and apoB should be evaluated and considered as secondary targets for lipid control.

According to the famous cardiovascular events chain proposed by Dzau and Braunwald, the development of CVD is a continuous process, and arterial stiffness is an important intermediate stage in this progression. Brachial-ankle pulse wave conduction velocity (baPWV) is a reliable method to screen for arterial stiffness, which is an independent predictor of cardiovascular morbidity and mortality and a valid surrogate endpoint for CVD [6–7]. Dyslipidemia is considered to be a possible risk factor for arterial stiffness [8–11], although the underlying mechanism is still unclear. Therefore, the target range and clinical value of controlling blood lipids for arterial stiffness are currently unclear. Most existing analyses of lipid discordance focus on the prediction and assessment of cardiovascular risk.

Is the relationship between arterial stiffness and blood lipids also affected by the discordance of lipid parameters? It is not yet clear whether discordance in lipid parameters provides additional clinical information on arterial stiffness. Therefore, the purpose of this study was to investigate the discordance between LDL-C and non-HDL-C or apoB in middle-aged and elderly Chinese individuals and assess the arterial stiffness risk among participants for whom these parameters were discordant.

# Methods

# Study population

This is a cross-sectional investigation analyzing baseline data collected for a prospective cohort study. The participants were middle-aged and elderly Northern Chinese patients who underwent annual physical examinations at Xuanwu Hospital of the Capital Medical University between July 2017 and October 2019.

The inclusion criteria for the study were as follows: (1) age 45 years or older, (2) underwent baPWV examination, and (3) no missing clinical and biochemical data. Patients with secondary hypertension, acute cardiovascular and cerebrovascular disease, severe arrhythmia, abnormal liver function (i.e., aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 100 U/L), abnormal kidney function (estimated glomerular filtration rate (eGFR) < 60mL/min/1.73 $m^2$), malignant tumor, infection, pregnancy and lactation, thyroid dysfunction, mental disease, and peripheral vascular disease (i.e., ankle/brachial systolic blood pressure index (ABI) < 0.9) were excluded. A total of 402 participants were included in the analysis.

All subjects provided informed consent prior to their participation in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Xuanwu Hospital, Capital Medical University.

# Data collection

Information on age, sex, smoking and alcohol consumption, medical history, and current drug use was collected using standardized questionnaires by trained physicians. Participants who smoked at least one cigarette per day or drank alcohol once a week for at least six months were defined as smokers or drinkers, respectively. Trained staff measured all participants' height in meters, weight in kilograms, and blood pressure in mmHg. The body mass index (BMI) was calculated as $kg/m^2$. An electronic sphygmomanometer was used to measure the participants' blood pressure in a seated position after a 10-minute rest. Triplicate measurements were taken with a break of at least 2 minutes between readings; the average value was used for the analysis.

Blood samples were collected in the morning after overnight fasting for at least 8 h. Fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), LDL-C, apoB, serum creatinine (Scr), uric acid(UA), and homocysteine levels were measured using an automatic biochemical analyzer (Olympus Corporation, Hitachi 7600, Japan). Non-HDL-C was calculated as TC minus HDL-C. EGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) method. Hemoglobin (HGB) levels were detected using an automatic blood cell analyzer (XE-2100, Hisemori Micon Company, Japan).

Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg on at least two blood pressure measurements per visit for at least two visits and/or prescription of any antihypertensive medication. Diabetes mellitus (DM) was defined as plasma glucose ≥ 7.0mmol/L for at least two measurements, glycosylated hemoglobin (HbA1C) ≥ 6.5%, or prescription of any antidiabetic medication.

The baPWV was measured using an oscillometer-based device (BP-203RPE III; Colin-Omron, Co., Ltd, Tokyo, Japan). Subjects underwent baPWV measurement after at least 5 min of rest in the supine position. Coffee, tea, cigarette use, or alcohol use were not allowed for 30 min before the test. Trained technicians and physicians placed pressure cuffs on both arms and ankles. The lower edge of the arm

cuff was positioned 2–3 cm above the cubital fossa transverse striation, while the lower edge of the ankle cuff was positioned 1–2 cm above the medial malleolus. The heartbeat monitor was placed on the left edge of the sternum, and the electrocardiogram electrodes were placed directly next to it. Two bilateral readings of baPWV measurements were taken simultaneously, and the maximum readings of the right and left baPWV were used for the analysis. The ABI and heart rate (HR) were recorded automatically.

# Statistical analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as proportions. Characteristics were compared between groups with significance tests using the chi-squared test for categorical variables or one-way analysis of variance (ANOVA) for continuous variables. According to the 2016 ESC / EAS guidelines for the management of dyslipidemia [12], the lipid goals for the very high-risk population were LDL-C < 1.81mmol/L, non-HDL-C < 2.59mmol/L, and apoB < 0.8mmol/L. As there was no standard cut-off point for discordance, we choose the above target values as the cut-off points (i.e., LDL-C: 1.81mmol/L, non-HDL-C: 2.59mmol/L, apoB: 0.80mmol/L) to define discordance, which was defined as LDL-C ≥ the cut-off point and non-HDL-C or apoB < the cut-off point or vice versa. Thus, participants were divided into four mutually exclusive concordance/discordance groups: low/low (LDL-C < the cut-off point and non-HDL-C or apoB < the cut-off point), low/high (LDL-C < the cut-off point and non-HDL-C or apoB ≥ the cut-off point), high/low (LDL-C ≥ the cut-off point and non-HDL-C or apoB < the cut-off point), and high/high (LDL-C ≥ the cut-off point and non-HDL-C or apoB ≥ the cut-off point). The characteristics of the groups were analyzed. The correlation between baPWV and LDL-C or non-HDL-C or apoB in the samples was performed using a Pearson analysis, and the correlation between discordant lipid patterns and the presence of arterial stiffness was performed using a Spearman analysis. All variables with $P < 0.05$ in univariate analysis or those considered clinically relevant (i.e., gender) were included in the logistic regression model to investigate the odds of arterial stiffness for each of the concordance/discordance groups, with the low/low group as the referent. Arterial stiffness was defined as the upper quartile of the baPWV. Statistical analysis was performed using SPSS (version 22.0; SPSS Inc., Chicago, USA), and a two-tailed P value < 0.05 was considered statistically significant.

# Results

The mean age of the study participants was 65.9 ± 13.0 years, and 59.5% of the participants were male. Of the patients, 77.6% had hypertension, 39.3% had diabetes, 39.8% were smokers, 25.6% were drinkers, and 44.8% were receiving lipid-lowering therapy. The mean LDL-C was 2.41 ± 0.81mmol/L, non-HDL-C 3.06 ± 0.94mmol/L, apoB 0.84 ± 0.21mmol/L, and baPWV 1,712.9 ± 405.8cm/s. The characteristics stratified according to the baPWV are shown in Table 1.

Table 1
Baseline characteristics of participants stratified according to baPWV

| Variables | Total | without AS | with AS | P |
|---|---|---|---|---|
| n | 402 | 301 | 101 | |
| Age, year | 65.9 ± 13.0 | 61.7 ± 11.3 | 78.5 ± 8.7 | 0.000 |
| Male, n (%) | 239 (59.5) | 181 (60.1) | 58 (57.4) | 0.632 |
| Smoking, n (%) | 160 (39.8) | 129 (42.9) | 31 (30.7) | 0.031 |
| Drinking, n (%) | 103 (25.6) | 88 (29.2) | 15 (14.9) | 0.004 |
| Hypertension, n (%) | 312 (77.6) | 219 (72.8) | 93 (92.1) | 0.000 |
| DM, n (%) | 158 (39.3) | 107 (35.5) | 51 (50.5) | 0.008 |
| SBP, mmHg | 130.1 ± 17.9 | 126.1 ± 16.2 | 142.1 ± 17.4 | 0.000 |
| DBP, mmHg | 75.0 ± 10.0 | 74.6 ± 9.6 | 76.1 ± 11.1 | 0.174 |
| BMI, $kg/m^2$ | 25.6 ± 3.4 | 25.8 ± 3.4 | 24.7 ± 3.3 | 0.004 |
| FBG, mmol/L | 5.9 ± 2.3 | 5.8 ± 2.2 | 6.3 ± 2.4 | 0.092 |
| HDL-C, mmol/L | 1.17 ± 0.31 | 1.17 ± 0.31 | 1.19 ± 0.33 | 0.477 |
| LDL-C, mmol/L | 2.41 ± 0.81 | 2.42 ± 0.83 | 2.36 ± 0.73 | 0.469 |
| Non-HDL-C, mmol/L | 3.06 ± 0.94 | 3.06 ± 0.99 | 3.06 ± 0.77 | 0.978 |
| TC, mmol/L | 4.23 ± 0.49 | 4.23 ± 0.98 | 4.25 ± 0.80 | 0.772 |
| TG, mmol/L | 1.84 ± 1.50 | 1.94 ± 1.63 | 1.54 ± 0.97 | 0.003 |
| apoB, mmol/L | 0.84 ± 0.21 | 0.84 ± 0.22 | 0.86 ± 0.16 | 0.354 |
| UA, μμmol/L | 348.6 ± 86.4 | 346.6 ± 83.7 | 354.7 ± 94.3 | 0.414 |
| homocysteine, mmol/L | 14.7 ± 7.7 | 14.5 ± 7.3 | 15.4 ± 8.9 | 0.276 |
| eGFR, mL/(min·1.73 $m^2$) | 91.1 ± 17.0 | 95.7 ± 14.4 | 77.3 ± 16.5 | 0.000 |
| HGB, g/L | 136.3 ± 15.6 | 138.0 ± 15.6 | 130.9 ± 14.4 | 0.000 |
| HR, bpm | 68.3 ± 9.6 | 67.4 ± 9.6 | 70.8 ± 9.1 | 0.002 |
| Lipid-lowering therapy, n (%) | 180 (44.8) | 124 (41.2) | 56 (55.4) | 0.013 |
| baPWV, cm/s | 1712.9 ± 405.8 | 1519.9 ± 225.0 | 2288.1 ± 249.0 | 0.000 |

LDL-C levels were positively correlated with non-HDL-C and apoB levels (r = 0.690 and r = 0.722, respectively), but there was discordance between them (Figs. 1 2). There were 285 participants (70.9%) with LDL-C ≥ 1.81mmol/L, 280 participants (69.7%) with non-HDL-C ≥ 2.59mmol/L, and 235 participants

(58.5%) with apoB ≥ 0.80mmol/L. Of the 285 participants with LDL-C ≥ 1.81mmol/L, 43 (15.1%) had lower non-HDL-C, and 87 (30.5%) had lower apoB than the cut-off point. Of the 117 participants with LDL-C < 1.81mmol/L, 38 (32.5%) had higher non-HDL-C, and 37 (31.6%) had higher apoB levels than the cut-off point. Overall, LDL-C was observed to be discordant with non-HDL-C (20.1%) and apoB (30.8%).

There were significant differences in the levels of SBP, DBP, LDL-C, non-HDL-C, TG, TC, apoB, baPWV, and the proportion of lipid-lowering drugs in the four concordance/discordance groups (Table 2 and Table 3). In the participants with non-HDL-C or apoB higher than the cut-off point, the levels of SBP, DBP, non-HDL-C, TG, TC, apoB, and baPWV were all increased while the proportion of lipid-lowering drugs was lower.

When stratified according to LDL-C levels, the baPWVs were greater in those with higher (≥

Table 2
Baseline characteristics of participants by LDL-C/Non-HDL-C concordance/discordance groups

| Variables | Low/Low | Low/High | High/Low | High/High | p |
|---|---|---|---|---|---|
| n | 79 | 38 | 43 | 242 | |
| Age, year | 65.1 ± 12.8 | 64.0 ± 15.1 | 65.6 ± 12.1 | 66.6 ± 12.9 | 0.596 |
| Male, n (%) | 52 (65.8) | 22 (57.9) | 28 (65.1) | 137 (56.6) | 0.432 |
| Smoking, n (%) | 32 (40.5) | 14 (36.8) | 17 (39.5) | 97 (40.1) | 0.983 |
| Drinking, n (%) | 27 (34.2) | 9 (23.7) | 14 (32.6) | 53 (21.9) | 0.114 |
| Hypertension, n (%) | 62 (78.5) | 25 (65.8) | 34 (79.1) | 191 (78.9) | 0.336 |
| DM, n (%) | 30 (38.0) | 14 (36.8) | 15 (34.9) | 99 (40.9) | 0.857 |
| SBP, mmHg | 122.7 ± 16.5 | 125.1 ± 16.4 | 124.8 ± 15.1 | 134.3 ± 17.8 | 0.000 |
| DBP, mmHg | 72.8 ± 10.9 | 72.1 ± 7.3 | 72.2 ± 8.1 | 76.6 ± 10.1 | 0.001 |
| BMI, $kg/m^2$ | 25.0 ± 3.2 | 25.6 ± 3.6 | 26.0 ± 2.7 | 25.7 ± 3.5 | 0.312 |
| FBG, mmol/L | 5.8 ± 2.3 | 5.9 ± 1.9 | 5.5 ± 1.5 | 6.0 ± 2.4 | 0.464 |
| HDL-C, mmol/L | 1.22 ± 0.35 | 1.09 ± 0.30 | 1.19 ± 0.31 | 1.17 ± 0.30 | 0.164 |
| LDL-C, mmol/L | 1.52 ± 0.22 | 1.58 ± 0.25 | 2.25 ± 0.63 | 2.85 ± 0.64 | 0.000 |
| Non-HDL-C, mmol/L | 1.89 ± 0.34 | 3.50 ± 0.79 | 2.27 ± 0.49 | 3.51 ± 0.70 | 0.000 |
| TC, mmol/L | 3.12 ± 0.47 | 4.59 ± 0.82 | 3.46 ± 0.58 | 4.68 ± 0.71 | 0.000 |
| TG, mmol/L | 1.34 ± 1.03 | 2.11 ± 2.18 | 1.19 ± 0.47 | 2.08 ± 1.56 | 0.000 |
| apoB, mmol/L | 0.58 ± 0.10 | 0.94 ± 0.15 | 0.71 ± 0.10 | 0.94 ± 0.16 | 0.000 |
| UA, μmol/L | 324.8 ± 76.2 | 354.7 ± 76.5 | 350.3 ± 89.2 | 355.2 ± 89.6 | 0.055 |
| homocysteine, mmol/L | 14.4 ± 7.0 | 14.2 ± 9.2 | 14.0 ± 5.0 | 15.0 ± 8.1 | 0.812 |
| eGFR, mL/(min·1.73 $m^2$) | 93.3 ± 16.3 | 94.5 ± 15.5 | 92.0 ± 14.7 | 89.6 ± 17.7 | 0.184 |
| HGB, g/L | 136.3 ± 14.7 | 135.1 ± 14.6 | 134.7 ± 13.3 | 136.7 ± 16.4 | 0.847 |
| HR, bpm | 67.6 ± 10.2 | 68.8 ± 9.2 | 65.4 ± 9.6 | 68.9 ± 9.5 | 0.148 |
| Lipid-lowering therapy, n (%) | 52 (65.8) | 19 (50.0) | 28 (65.1) | 81 (33.5) | 0.000 |
| baPWV, cm/s | 1533.0 ± 330.9 | 1713.3 ± 604.8 | 1605.4 ± 221.4 | 1790.7 ± 393.8 | 0.000 |

Table 3
Baseline characteristics of participants by LDL-C/apoB concordance/discordance groups

| Variables | Low/Low | Low/High | High/Low | High/High | p |
|---|---|---|---|---|---|
| n | 80 | 37 | 87 | 198 | |
| Age, year | 64.7 ± 12.8 | 64.8 ± 15.1 | 66.5 ± 13.6 | 66.4 ± 12.4 | 0.684 |
| Male, n (%) | 52 (65.0) | 22 (59.5) | 50 (57.5) | 115 (58.1) | 0.725 |
| Smoking, n (%) | 32 (40.0) | 14 (37.8) | 32 (36.8) | 82 (41.4) | 0.895 |
| Drinking, n (%) | 27 (33.8) | 9 (24.3) | 24 (27.6) | 43 (21.7) | 0.206 |
| Hypertension, n (%) | 63 (78.8) | 24 (64.9) | 65 (74.7) | 60 (80.8) | 0.164 |
| DM, n (%) | 31 (38.8) | 13 (35.1) | 28 (32.2) | 86 (43.4) | 0.315 |
| SBP, mmHg | 122.3 ± 16.3 | 126.2 ± 16.7 | 128.9 ± 15.8 | 134.6 ± 18.3 | 0.000 |
| DBP, mmHg | 72.5 ± 10.6 | 72.8 ± 8.2 | 73.8 ± 9.8 | 76.9 ± 9.9 | 0.002 |
| BMI, $kg/m^2$ | 25.0 ± 3.1 | 25.5 ± 3.8 | 25.3 ± 3.1 | 25.9 ± 3.5 | 0.236 |
| FBG, mmol/L | 5.9 ± 2.4 | 5.8 ± 1.7 | 5.6 ± 1.8 | 6.1 ± 2.5 | 0.237 |
| HDL-C, mmol/L | 1.22 ± 0.35 | 1.19 ± 0.30 | 1.23 ± 0.34 | 1.15 ± 0.29 | 0.054 |
| LDL-C, mmol/L | 1.51 ± 0.22 | 1.59 ± 0.25 | 2.29 ± 0.45 | 2.97 ± 0.66 | 0.000 |
| Non-HDL-C, mmol/L | 1.93 ± 0.44 | 3.46 ± 0.81 | 2.61 ± 0.39 | 3.64 ± 0.74 | 0.000 |
| TC, mmol/L | 3.15 ± 0.51 | 4.56 ± 0.86 | 3.83 ± 0.48 | 4.79 ± 0.76 | 0.000 |
| TG, mmol/L | 1.48 ± 1.62 | 1.82 ± 1.34 | 1.49 ± 0.76 | 2.14 ± 1.67 | 0.000 |
| apoB, mmol/L | 0.58 ± 0.10 | 0.95 ± 0.15 | 0.72 ± 0.06 | 0.98 ± 0.15 | 0.000 |
| UA, μmol/L | 343.6 ± 75.5 | 358.0 ± 76.7 | 346.8 ± 90.4 | 357.8 ± 89.0 | 0.062 |
| homocysteine, mmol/L | 14.3 ± 7.0 | 14.4 ± 9.3 | 14.7 ± 7.0 | 14.9 ± 8.0 | 0.946 |
| eGFR, $mL/(min·1.73\ m^2)$ | 94.2 ± 15.6 | 92.7 ± 16.8 | 90.4 ± 16.4 | 89.8 ± 17.7 | 0.232 |
| HGB, g/L | 136.7 ± 14.0 | 135.3 ± 16.1 | 135.9 ± 15.4 | 136.4 ± 15.9 | 0.060 |
| HR, bpm | 67.4 ± 9.7 | 68.3 ± 10.1 | 66.9 ± 8.7 | 68.4 ± 9.7 | 0.064 |
| Lipid-lowering therapy, n (%) | 54 (67.5) | 17 (45.9) | 39 (44.8) | 70 (35.4) | 0.000 |
| baPWV, cm/s | 1525.7 ± 327.0 | 1733.9 ± 609.4 | 1684.0 ± 364.2 | 1797.3 ± 380.4 | 0.000 |

2.59mmol/L) compared to those with lower (< 2.59mmol/L) non-HDL-C levels (LDL-C < 1.81mmol/L: 1,713.3 ± 604.8cm/s versus 1,533.0 ± 330.9cm/s, p = 0.039; LDL-C ≥ 1.81mmol/L: 1,790.7 ± 393.8cm/s versus 1,605.4 ± 221.4cm/s, p = 0.000; Table 4). Similar trends were observed in those with higher (≥ 0.80mmol/L) compared to those with lower (< 0.80mmol/L) apoB levels (LDL-C < 1.81mmol/L: 1,733.9 ± 609.4cm/s versus 1,525.7 ± 327.0cm/s, p = 0.018; LDL-C ≥ 1.81mmol/L: 1,797.3 ± 380.4cm/s versus 1,684.0 ± 364.2cm/s, p = 0.020; Table 5).

Table 4
baPWV of participants by LDL-C/Non-HDL-C concordance/discordance groups

| Groups, mmol/L | LDL < 1.81 | | LDL ≥ 1.81 | |
|---|---|---|---|---|
| | Non-HDL-C < 2.59 | Non-HDL-C ≥ 2.59 | Non-HDL-C < 2.59 | Non-HDL-C ≥ 2.59 |
| n | 79 | 38 | 43 | 242 |
| baPWV, cm/s | 1533.0 ± 330.9 | 1713.3 ± 604.8 | 1605.4 ± 221.4 | 1790.7 ± 393.8 |
| F | 2.953 | | 19.278 | |
| P | 0.039 | | 0.000 | |

Table 5
baPWV of participants by LDL-C/apoB concordance/discordance groups

| Groups, mmol/L | LDL < 1.81 | | LDL ≥ 1.81 | |
|---|---|---|---|---|
| | apoB < 0.8 | apoB ≥ 0. 8 | apoB < 0.8 | apoB ≥ 0.8 |
| n | 80 | 37 | 87 | 198 |
| baPWV, cm/s | 1525.7 ± 327.0 | 1733.9 ± 609.4 | 1684.0 ± 364.2 | 1797.3 ± 380.4 |
| F | 5.781 | | 5.509 | |
| P | 0.018 | | 0.020 | |

The Spearman analysis showed a significant association between discordant lipid patterns and the presence of arterial stiffness (LDL-C/non-HDL-C:r = 0.131, p = 0.008; LDL-C/apoB: r = 0.117, p = 0.019). Table 6 displays the ORs of arterial stiffness for the four concordance/discordance groups of each set of LDL-C and non-HDL-C or apoB groups separately after adjusting for age, sex, smoking, drinking, hypertension, diabetes, SBP, TG, eGFR, HGB, lipid-lowering therapy, BMI, and HR. The low/low groups constituted the referent in the logistic regression model. The ORs of the high LDL-C/low non-HDL-C and high LDL-C/low apoB groups were not significantly higher than the referent. In contrast, the ORs of the low LDL-C/high non-HDL-Cand low LDL-C/high apoB groups were significantly higher than the referent. The high LDL-C/high non-HDL-C and high LDL-C/high apoB groups were also significantly higher than those in the referent.

Table 6
Concordance/Discordance between LDL-C and Non-HDL-C or apoB groups in relation to the arterial stiffness risk

| LDL-C/Non-HDL-C | OR (95% CI) | P | LDL-C/apoB | OR (95% CI) | P |
|---|---|---|---|---|---|
| Low/Low (referent) | 1 | 0.001 | Low/low (referent) | 1 | 0.005 |
| Low/High | 13.412 (2.341–76.850) | 0.004 | Low/high | 13.054 (2.385–71.454) | 0.003 |
| High/Low | 0.268 (0.044–1.618) | 0.151 | High/low | 1.214 (0.408–3.609) | 0.727 |
| High/High | 3.174 (1.219–8.262) | 0.018 | High/high | 3.062 (1.147–8.179) | 0.026 |

# Discussion

The study was conducted in a population of middle-aged and elderly Chinese individuals, who are known to have a high prevalence of arterial stiffness. The lipid goal for the very high-risk population according to the 2016 ESC/EAS Guidelines was also the ninth National Health and Nutrition Examination Survey (NHANES) percentile, which was chosen as the cut-off point in this study. According to this, LDL-C was discordant with non-HDL-C (20.1%) and apoB (30.8%), which were higher than the results of the study by Lawler PR et al [13] and the study by Wilkins JT et al [14]. Lower non-HDL-C and apoB levels were associated with lower baPWV, whereas higher non-HDL-C and apoB levels were associated with higher baPWV. In the discordant groups, the odds for arterial stiffness were significantly higher when non-HDL-C or apoB was greater than the cut-off point and not significantly higher than the referent when non-HDL-C or apoB was below the cut-off point, suggesting that the risk for arterial stiffness is more strongly influenced by non-HDL-C or apoB than by LDL-C. Notably, participants with high LDL-C and high non-HDL-C or apoB also had high risks for arterial stiffness, the particles of which were numerous but of an average cholesterol concentration. These results suggested that only patients with non-HDL-C or apoB higher than the cut-off point had an increased risk of arterial stiffness; thus, the increased risk of arterial stiffness may be due to the significant differences in non-HDL-C or apoB among the groups. In addition, there was a trend toward a high arterial stiffness risk in the discordant groups with low non-HDL-C or apoB and high LDL-C, possibly because their non-HDL-C and apoB increased by 0.38 mmol/L and 0.14mmol/L, respectively, compared with the referent.

Arterial stiffness measured by baPWV is considered a marker of subclinical atherosclerosis and an independent risk predictor of CVD [15]. Therefore, the identification of serum biomarkers associated with arterial stiffness will have great advantages in preventing atherosclerosis and CVD and have substantial clinical benefits. In the case of similar blood pressure and age, arterial stiffness in patients with hypercholesterolemia was more serious than that in patients with normal blood lipid levels [16]. In addition, several clinical trials have shown that lipid-lowering therapy can improve the baPWV [17]. Thus,

there was a correlation between dyslipidemia and arterial stiffness. LDL-C has long been the major target of lipid-lowering therapies, while non-HDL-C and apoB are still controversial targets. Nevertheless, many studies have confirmed the effect of non-HDL-C or apoB on arterial stiffness. Furthermore, a Dutch study involving 1,517 participants supported the use of non-HDL-C as a superior predictor of LDL-C in identifying individuals with arterial stiffness [18]. A recent meta-analysis of 303 participants by Upala et al. [19] also reported an association between statin therapy and the PWV in the lower aortic segment. In several studies from China [20–21], non-HDL-C was more strongly associated with the baPWV than other lipid parameters. This correlation was significant in both men and women, suggesting that non-HDL-C was a surrogate lipid marker of the arterial stiffness level. In a study of patients with familial hypobetalipoproteinemia (FHBL) [22], an attenuated gradual increase in arterial stiffness was found, and lowering of apoB-containing lipoproteins should have a beneficial impact on the vascular system in subjects with “non-cholesterol” risk factors. An NBS (Nijmegen Biomedical Study) study had shown that an elevated apoB level was a marker of more severe arterial stiffness [23]. Studies from South Korea [24] and Finland [25] showed that elevations of apoB or non-HDL-Care associated with increased arterial stiffness in young adults, and an increase in apoB could lead to an increase in arterial stiffness. A study on adolescents with type 1 diabetes had found that elevated apoB was significantly associated with increased arterial stiffness, especially in those with borderline LDL-C (2.59–3.34mmol/L), and apoB in addition to LDL-C might help stratify the CVD risk [26].

This study had several limitations. First, the cross-sectional study might have selection bias, and the sample size was small; therefore, participants in this study might not represent the general middle-aged and elderly population. Second, nearly half of the participants in the study were receiving lipid-lowering therapy, which could affect the relationship between blood lipids and arterial stiffness. Finally, there is no absolute definition and no standard cut-off point for discordance between LDL-C, non-HDL-C, and apoB; therefore, changing the definition and cut-off point could affect the results.

# Conclusions

In conclusion, non-HDL-C or apoB is not discordant with LDL-C in middle-aged and elderly Chinese, which can significantly affect arterial stiffness. Lipid-lowering therapy in middle-aged and elderly individuals should not only focus on LDL-C levels, but also on non-HDL-C and apoB levels to further reduce arterial stiffness. We conducted a study and discussion to analyze the effect of the discordance between non-HDL-C or apoB and LDL-C on arterial stiffness, showing that non-HDL-C or apoB can further affect arterial stiffness on the basis of LDL-C and reclassified the risk of arterial stiffness. When discordant with LDL-C, non-HDL-C or apoB may identify individuals who may benefit from more intensive lipid modification. Further large studies are required to study the discordance patterns and new lipid targets are required to set.

# Abbreviations

| apolipoprotein B | apoB |
|---|---|
| aspartate aminotransferase | AST |
| alanine aminotransferase | ALT |
| ankle/brachial systolic blood pressure index | ABI |
| brachial-ankle pulse wave conduction velocity | baPWV |
| body mass index | BMI |
| cardiovascular disease | CVD |
| Chronic Kidney Disease Epidemiology Collaboration | CKD-EPI |
| diastolic blood pressure | DBP |
| Diabetes mellitus | DM |
| estimated glomerular filtration rate | eGFR |
| European Society of Cardiology / European Atherosclerosis Society | ESC / EAS |
| fasting blood glucose | FBG |
| familial hypobetalipoproteinemia | FHBL |
| glycosylated hemoglobin | HbA1C |
| high-density lipoprotein cholesterol | HDL-C |
| hemoglobin | HGB |
| heart rate | HR |
| low-density lipoprotein cholesterol | LDL-C |
| lipoprotein a | LPa |
| non-high-density lipoprotein cholesterol | non-HDL-C |
| National Health and Nutrition Examination Survey | NHANES |
| one-way analysis of variance | ANOVA |
| serum creatinine | Scr |
| systolic blood pressure | SBP |
| total cholesterol | TC |
| triglyceride | TG |
| uric acid | UA |

# Declarations

### *Ethics approval and consent to participate*

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee of Xuanwu Hospital, Capital Medical University (Clinical research review [2018] No. 038, July 10, 2018) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants involved in the study.

### *Consent for publication*

All participants provided consent for publication.

### *Availability of data and materials*

The data underlying this article will be shared on reasonable request to the corresponding author.

### *Competing interests*

The authors declare that they have no competing interests.


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There were no external funding sources for this study.


### *Authors' contributions*

All the authors listed in the manuscript participated in the design of the study and writing of the manuscript. GQ and ZZ performed the statistical analysis. All authors read and approved the final manuscript.


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# Figures

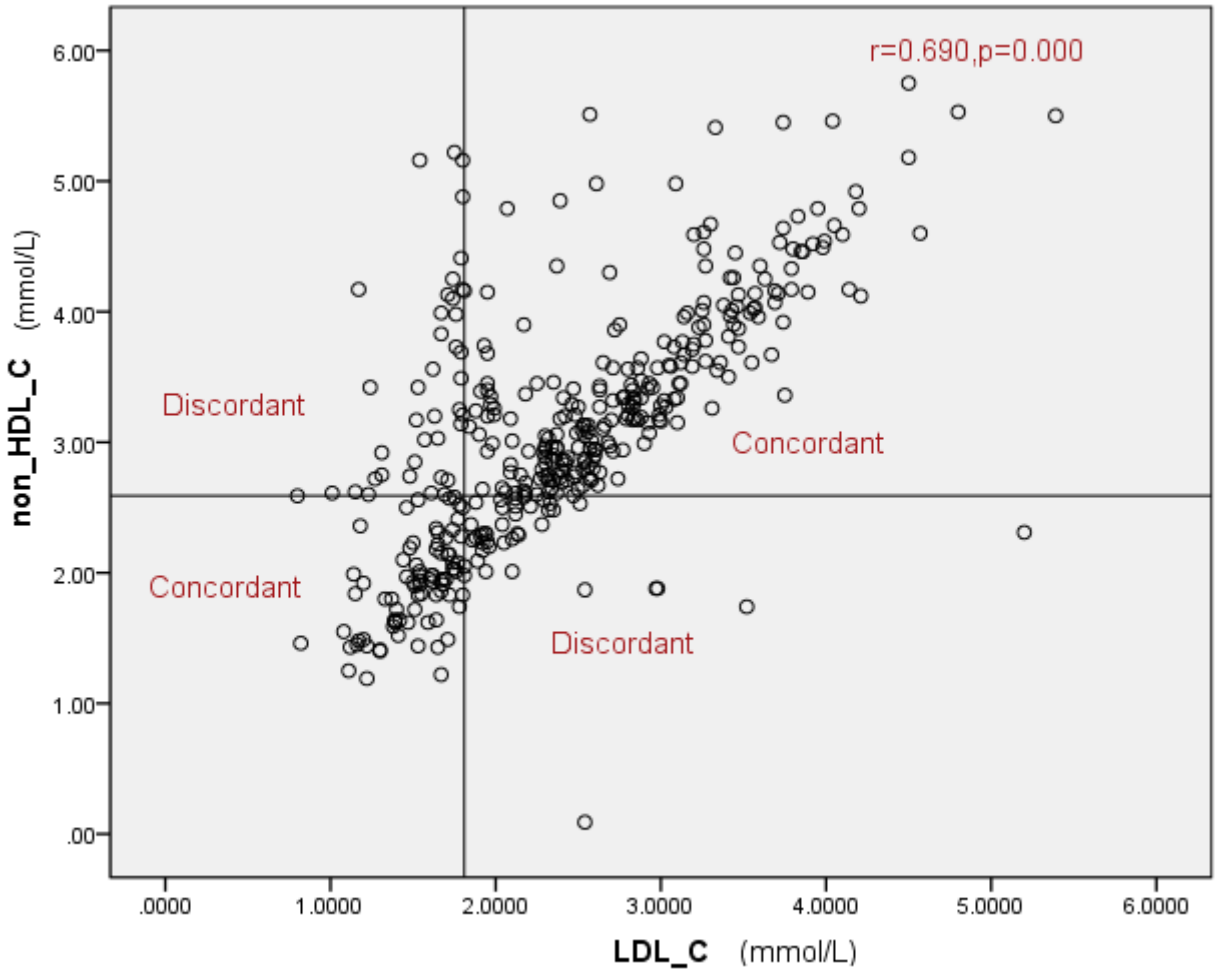
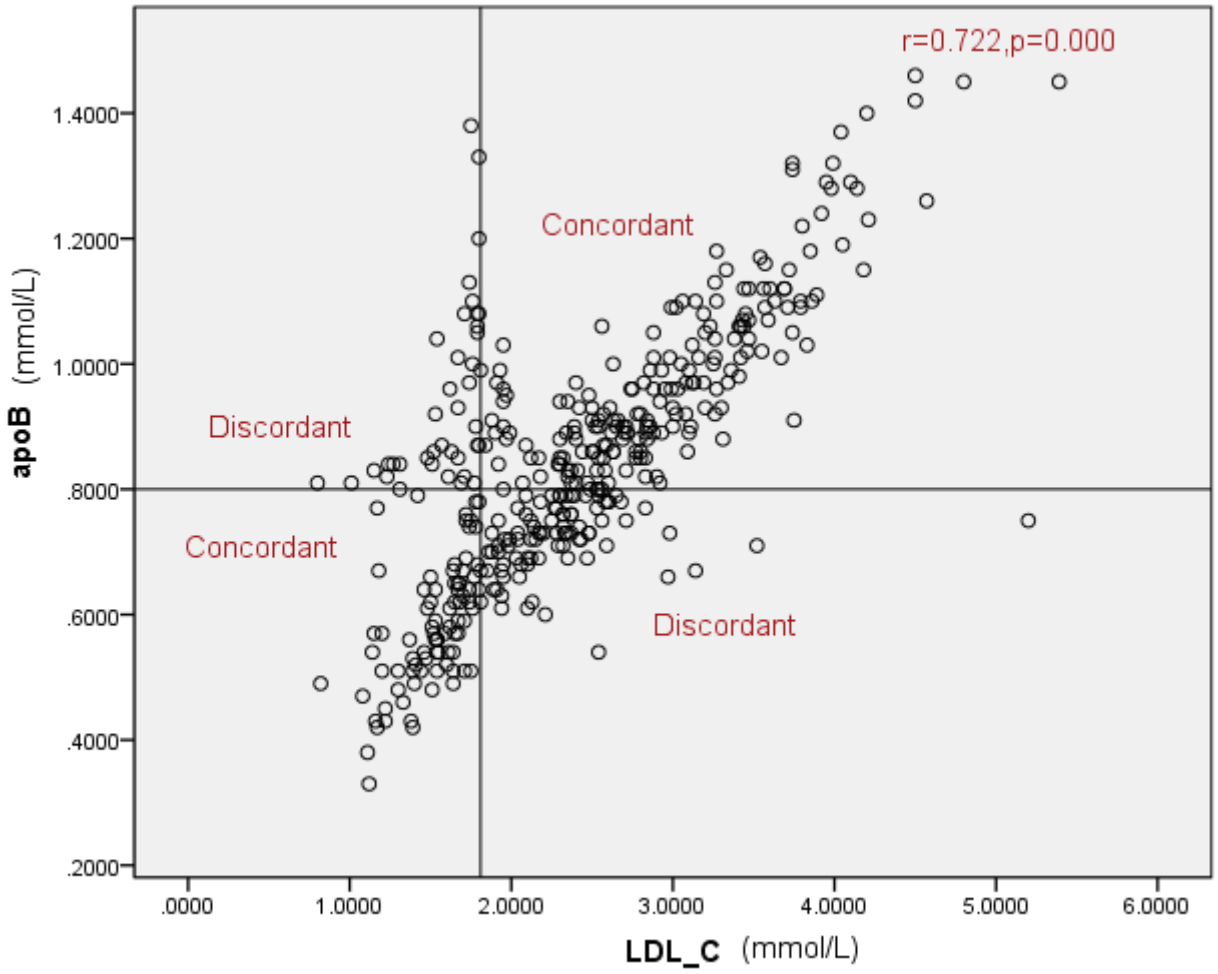



**Figure 1**

Scatterplots and discordance and concordance prevalence, according to the cut-off points of LDL-C and non-HDL-C.




## Figure 2

Scatterplots and discordance and concordance prevalence, according to the cut-off points of LDL-C and apoB.