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Association of Carotid Intima-Media Thickness and Plague with Lipid Profiles in a High-Stroke-Risk Population

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Objective: This study aimed to determine the relationship between lipid profiles, carotid intima-media thickness and plaques in a Mongolian high-stroke-risk population. **Methods:** A hospital-based cross-sectional study was conducted with Mongolian adults who underwent interviews, physical examinations, and laboratory testing from May through November 2022 at the Mongolia-Japan and Enerel hospitals. The subjects with a high risk of stroke were selected according to Framingham Stroke Risk Score (FSRS). Carotid ultrasonography was then performed on the high-stroke-risk participants. **Results:** Overall, 78 subjects with a high risk of stroke out of 280 participants were ultimately included in the analysis. Carotid plaques were identified in 43 (55.1 %) and thickened cIMT in 68 (87.2 %). Multivariate regression analysis demonstrated that non-HDL-C ($B = 0.434$, $p < 0.05$) was an independent determinant of cIMT, whereas non-HDL-C/HDL-C (OR 8.335, 95 % CI, 2.984 - 23.287, $p = 0.009$) and LDL-C (OR 9.085, 95 % CI, 1.490 - 55.409, $p = 0.017$) had the strongest association with carotid plague. **Conclusions:** These findings indicate that non-HDL-C was an independent risk factor for cIMT. Among the lipid profiles, non-HDL-C/HDL-C ratio and LDL-C level have the strongest association with carotid plaques in the Mongolian high-stroke-risk population.

Keywords: carotid artery plaque, lipids, low-density lipoprotein cholesterol, stroke, atherosclerosis

Introduction

Carotid atherosclerosis (CA) is the leading cause of cerebral infarction [1]. Carotid plaque detected by ultrasound can not only identify the severity of carotid artery stenosis and morphological changes of atherosclerosis but also can be a subclinical indicator of CA and predict the risk of ischemic stroke [2 - 5]. In addition, studies have shown that carotid artery intima-media thickness (cIMT) is an early indicator of atherosclerosis, with the odds ratio for heart attack and stroke 1.09 for a 0.1 mm increase in cIMT [6, 7]. The results of several studies examining the relationship of atherosclerosis to blood lipid parameters in different populations have varied [8 - 11]. Among lipid profiles, most predictive of CA were non-high-density lipoprotein cholesterol (non-HDL-C),

high-density lipoprotein cholesterol (HDL-C) and the ratio of total cholesterol (TC) to HDL-C (TC/HDL-C) [1, 8, 10]. Many risk factors for cardiovascular disease (CVD) and stroke have been identified, but data on their predictive values for early-stage asymptomatic atherosclerosis remain limited. For people at risk of CVD and stroke, it is clear that prevention of atherosclerosis in its early stages is an effective way to prevent ischemia. Previous studies have indicated a high prevalence of dyslipidemia (47.9 %), low level of awareness, insufficient treatment among the adults aged 20 - 69 in Ulaanbaatar relative to some other countries and some relationships between dyslipidemia and stroke. However, the relationship between lipid parameters and carotid plaques is still largely unexplored in different populations. Therefore, the purpose of our study was to detect the relevant factors of cIMT and carotid plaque in high-stroke-risk Mongolian adults and analyze the predictive values of different risk factors, including different lipid profiles, for cIMT and the presence of carotid plaque.

Materials and Methods

Study population

A cross-sectional study of 280 participants aged 55 - 85 without previous history of acute stroke recruited from Enerel and Mongolia-Japan Hospitals (outpatients and inpatients) from May through November 2022 were included in this study. High-stroke-risk participants were identified and underwent carotid ultrasound. Participants with a diagnosis of acute myocardial infarction, stroke, heart failure, peripheral arterial disease, end-stage renal disease or malignant tumor and participants on lipid-lowering therapy were excluded.

Data collection

Demographic, clinical characteristics and stroke risk assessment

Demographic data, including age, sex, and smoking status were collected using a specially designed questionnaire. Smokers were defined as those currently smoking or within 1 year of quitting. Body mass index (BMI) was calculated by the equation BMI = weight (kg) / height $(m)^2$. Blood pressure was measured with a standard sphygmomanometer in a sitting position after ten minutes of rest (mmHg). Hypertension was defined as a systolic blood pressure greater than 130 mmHg or a diastolic blood pressure greater than 80 mmHg or the use of antihypertensive medication. Determination of atrial fibrillation was by cardiologist's diagnosis or ECG evidence, and left ventricular hypertrophy (LVH) was based on ECG evidence. Diabetes was defined according to the 1999 revised WHO criteria: fasting plasma glucose level ≥ 126 mg/dL (7.0 mmol/L); A plasma glucose level ≥ 200 mg/dL (11.1 mmol/L) 2 hours after oral administration of 75 g of glucose. People who used antidiabetic drugs were also defined as having diabetes. Stroke risk was assessed using the Framingham Stroke Risk Score (FSRS) of the American Heart Association [12]. It uses age, sex, systolic blood pressure, diabetes, smoking, previous CVD (history of prior heart attack, coronary heart disease, heart failure, and peripheral vascular disease), atrial fibrillation, and coronary artery disease, with left ventricular hypertrophy and the use of antihypertensive drugs to calculate the risk of acute stroke within 10 years. Numerous studies have confirmed the validity and reliability of the FSRS criteria. If the FSRS is less than 10%, the stroke risk is low, 10 % - 19 % is medium, and 20 % or more are at high risk [13].

Laboratory examination

Venous blood samples were collected from each participant early in the morning. Blood lipid fractions (total cholesterol-TC, triglyceride-TG, LDL-C, HDL-C) were determined by an automatic analyzer (COBAS INTEGRA 400 PLUS, Roche, 2009). Normal reference ranges were 0.56 - 1.70 mmol/L for TG, 2.8 - 5.9 mmol/L for TC, 2.07 - 3.36 mmol/L for LDL-C, 0.90 - 1.55 mmol/L for HDL-C [14, 15]. The value of non-HDL-C was obtained by subtracting HDL-C from the TC level [16]. Non-HDL-C/HDL-C, TG/HDL-C and LDL-C/HDL-C ratios were calculated accordingly.

Carotid ultrasonography

Measurements of the right and left carotid arteries with a 7.5 MHz linear transducer of a high-resolution vascular ultrasound machine (Samsung Accuvix XG 4D device) were performed by two qualified sonographers independent of the clinical characteristics of the participants. Images of the extracranial carotid artery were analyzed in longitudinal (anterior, lateral, and posterior views) and transverse planes, common carotid artery (CCA), internal carotid artery (ICA), and external carotid artery (ECA) on both sides in multiview B-mode imaging. The distance between the media-adventitia and lumen-intima boundaries was quantified at plaque-free sections of the carotid artery and defined as cIMT,

and three measurements were taken on the right and left side, and the thickest dimension was recorded. cIMT > 0.9 mm was defined as thickened cIMT [17]. Carotid plaque was defined as a focal cIMT ≥ 1.5 cm or a discrete structure protruding into the arterial lumen more than 50% from the surrounding cIMT, based on the American Society of Echocardiography [18].

Statistical analysis

Statistical analysis was performed using SPSS 24.0 (IBM SPSS, Chicago, USA). Continuous variables are presented as mean (standard deviation) where normal and range when not normal. Categorical variables are presented as numbers (percentages). The normal distribution of continuous variables was confirmed by the Kolmogorov-Smirnov test, and the t-test, Mann-Whitney U test, or Chi-square test were used to compare data between groups. Spearman's rank correlation assessed the linear relationship between cIMT and clinical characteristics (lipid parameters, etc.). Univariate and multivariate linear regression models were performed to investigate factors associated with cIMT. Univariate and multivariate logistic regression models (Backward LR) were performed to examine independent predictors of carotid plaque. Results were considered statistically significant when $p < 0.05$.

Ethical statement

The permission to conduct the research was obtained from the Ethical Review Committee of MNUMS (#2022/3-05), and the research was carried out with the consent of the participants through the identification sheet. The researchers maintained the confidentiality of the participants.

Results

Of the 280 Mongolian adults enrolled, 78 (27.9 %) participants were high-stroke risk (FSRS mean 19.06 ± 4.45, 31.01 ± 10.04 %) consisting of 40 men and 38 women, ages 56 - 84 years (mean age 69.88 ± 8.04). The baseline characteristics of the study participants with high-stroke risk are shown in Table 1. The mean cIMT was 1.20 mm, and plaque was detected in 43 participants (55.1 %). Of all participants, 73 (93.6 %) had arterial hypertension, 77 (98.7 %) had CVD, 24 (30.8 %) had left ventricular hypertrophy, and smoking was significantly more prevalent in men than in women (28.2 % vs. 9.0 %, $p < 0.05$).

As shown in Table 2, the levels of TC, TG, LDL-C, and non-HDL-C and the ratios LDL-C/HDL-C, TG/HDL-C and non-HDL-C/HDL-C were statistically significantly higher in the group with carotid plague compared to the group without carotid plaque. In addition, parameters such as male gender, smoking rate, mean age, and BMI were different between the group with and without carotid plaque. cIMT was not normally distributed and was greater in the group with carotid plaque than in the group without carotid plaque (1.50 (0.60, 2.10) vs. 1.10 (0.14, 2.00) mm, $p < 0.001$). Based on the cutoff level of 0.9 mm, the percentage of people with a thickened cIMT was 87.2 %. As seen in Table 3, TG, non-HDL-C, TG/HDL-C and non-HDL-C/HDL-C ratios were significantly different between the normal and thickened cIMT groups. The results of Spearman's correlation analysis are shown in Table 4.

Among the lipid parameters, TC, TG, non-HDL-C ($r = 0.346$, 0.340 and 0.408, $p < 0.05$) and TG/HDL-C, LDL-C/HDL-C and non-HDL-C ratios ($r = 0.351$, 0.270, and 0.369, $p < 0.05$) were significantly correlated with the mean cIMT (Table 4 and Figure 1). The results of the univariate linear regression analysis are presented in Table 5. Among lipid parameters, TC (standard B = 0.371, $p = 0.001$), TG (standard B = 0.362, $p = 0.001$), non-HDL-C (standard B = 0.447, $p < 0.001$) and TG/HDL-C, non-HDL-C/ HDL-C (standard B = 0.311, 0.410 $p < 0.001$) were more closely associated with mean cIMT than other lipid parameters in a univariate linear regression model.

Subsequently, multiple linear regression analysis was performed using all the statistically significant variables in the univariate linear regression analyses as independent variables and the log-transformed cIMT as the dependent variable. The non-HDL-C level (standard B = 0.434, $p < 0.05$) was determined as an independent factor (Table 6). The results of the univariate logistic regression analysis are presented in Table 7. Among the parameters of atherogenic lipids, TC (OR 0.365, 95 % CI 0.218 - 0.611, $p = 0.000$), TG (OR 0.205, 95 % CI 0.088 - 0.478, $p = 0.000$) non-HDL-C (OR 0.338, 95 % CI 0.197 - 0.577, $p = 0.000$) and LDL-C (OR 0.616, 95 % CI 0.439 - 0.863, $p = 0.005$), were more closely associated with the development of carotid plaques. A stepwise multivariate logistic regression analysis was

performed using all variables with a significance value of less than 0.05 as the independent variable and carotid plaque as the dependent variable in the univariate regression model. As shown in Table 8, multivariate logistic regression analysis showed that LDL-C (OR 9.085, 95 % CI 1.490 - 55.409, p = 0.017) and non-HDL-C/HDL-C ratio were independent predictors of carotid plaque development (OR 8.335, 95 % CI 2.984 - 23.287, p = 0.009). Multicollinearity diagnostics were performed and checked variance inflation factor (VIF) with all statistically significant independent variables (TC 3.297, TG 1.465, LDL-C 4.799, LDL-C/HDL-C 4.775, non-HDL-c 4.015, non-HDL-C/HDL 3.886, TG/HDL-C 2.676) in the univariate logistic regression and all the variables included multivariate logistic regression analysis.

Table 1. Characteristics of study participants (n = 78).

Variables	Men (n = 40)	Women (n = 38)	Total (n = 78)	P-value
Age (± SD), years	69.10 ± 6.45	70.71 ± 9.48	69.88 ± 8.04	0.380
BMI (± SD), Kg/m^2	27.28 ± 4.69	29.38 ± 7.45	28.30 ± 6.24	0.137
FSRS (± SD)	19.39 ± 5.82	18.71 ± 2.25	19.06 ± 4.45	0.500
FSRS (%)	31.87 ± 11.16	30.10 ± 8.77	31.01 ± 10.04	0.439
TC (mmol/L)	5.39 ± 1.18	5.85 ± 1.21	5.62 ± 1.21	0.089
TG (mmol/L)	1.90 ± 1.86	2.10 ± 1.15	2.00 ± 1.54	0.566
HDL-C (mmol/L)	1.56 ± 0.39	1.55 ± 0.42	1.56 ± 0.40	0.923
LDL-C (mmol/L)	4.84 ± 1.76	4.83 ± 1.72	4.84 ± 1.73	0.997
Non-HDL-C (mmol/L)	3.83 ± 1.16	4.30 ± 1.12	4.06 ± 1.16	0.070
LDL-C/ HDL-C	3.16 ± 0.95	3.19 ± 1.09	3.17 ± 1.01	0.882
Non-HDL-C/ HDL-C	2.63 ± 1.11	2.97 ± 1.12	2.79 ± 1.12	0.192
TG/ HDL-C	1.29 ± 1.18	1.46 ± 0.83	1.37 ± 1.02	0.547
SBP (mmHg)	150.38 ± 19.98	150.26 ± 18.42	150.32 ± 19.11	0.980
DBP (mmHg)	90.5 (60,110)	91 (55,103)	91 (55,110)	0.934
Smoking, n (%)	22 (28.2)	7 (9.0)	29 (37.2)	0.001*
Diabetes, n (%)	11 (14.1)	15 (19.2)	26 (33.3)	0.338
Hypertension, n (%)	37 (47.4)	36 (46.2)	73 (93.6)	0.988
CVD, n (%)	40 (51.3)	37 (47.4)	77 (98.7)	0.487
AF, n (%)	5 (6.4)	5 (6.4)	10 (12.8)	1.000
LVH, n (%)	13 (16.7)	11 (14.1)	24 (30.8)	0.809
cIMT (mm)	1.30 (0.14, 2.10)	1.15 (0.60, 2.10)	1.20 (0.14, 2.10)	0.374
Carotid plague	23 (29.5)	20 (25.6)	43 (55.1)	0.820

[a]The t-test, Fisher's test, and the $\chi 2$ test were used to compare proportions, *p < 0.05, SD - Standard deviation, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure, TC - total cholesterol, TG - triglyceride, LDL-C - low-density lipoprotein cholesterol, HDL-C - high-density lipoprotein cholesterol, Non-HDL-C - non-high-density lipoprotein cholesterol, CVD - cardiovascular disease, AF - atrial fibrillation, LVH - left ventricular hypertrophy, cIMT - carotid intima-media thickness.

Table 2. Characteristics of participants between groups with and without carotid plaque.

Variables	Plague (+) (n = 43)	Plague (-) (n = 34)	[a]P-value
Age, (±SD), years	70.37 ± 8.57	69.29 ± 7.43	0.551
Sex (Male: female)	23 (29.5): 20 (25.6)	17 (21.8): 18 (23.1)	0.820
BMI (±SD), Kg/m^2	29.29 ± 6.96	27.09 ± 5.06	0.111
Smoking	15 (19.2)	14 (17.9)	0.814
SBP (mmHg)	152 (90, 182)	151 (112, 192)	0.924
DBP (mmHg)	90.0 (60, 110)	93 (55, 103)	0.828
TC (mmol/L)	6.14 ± 1.09	4.98 ± 1.03	0.000*
TG (mmol/L)	2.50 ± 1.89	1.40 ± 0.60	0.001*
HDL-C (mmol/L)	1.56 ± 0.35	1.55 ±0.46	0.976
LDL-C (mmol/L)	5.38 ± 1.79	4.19 ± 1.41	0.002*
non-HDL-C (mmol/L)	4.59 ± 1.04	3.43 ± 0.97	0.000*
LDL-C/ HDL-C	3.52 ± 1.09	2.76 ± 0.74	0.001*
TG/ HDL-C	1.69 ± 1.22	0.99 ± 0.51	0.001*
Non-HDL-C/ HDL-C	3.11 ± 1.05	2.42 ± 1.10	0.007*
cIMT (mm)	1.50 (0.60, 2.10)	1.10 (0.14, 2.00)	0.000*

[a]The t-test, Fisher's test, and the T 2 test were used to compare proportions, *p < 0.05, SD - Standard deviation, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure, TC - total cholesterol, TG - triglyceride, LDL-C - low-density lipoprotein cholesterol, HDL-C - high-density lipoprotein cholesterol, Non-HDL-C -non-high-density lipoprotein cholesterol, cIMT - carotid intima-media thickness.

Table 3. Characteristics of participants between groups with normal and thickened intima- media thickness.

Characteristics	Normal (cIMT ≤ 0.9 mm) (n = 10)	Thickened (cIMT > 0.9 mm) (n = 68)	[a]P-value
Age (years)	69.60 ± 9.85	69.93 ± 7.83	0.922
Sex (Male: female)	4 (5.1): 6 (7.7)	36 (46.2): 32 (41)	0.512
BMI (± SD), kg/m^2	25.5 ± 4.51	28.71 ± 6.38	0.066
Smoking	3 (3.8)	26 (33.3)	0.736
SBP (mmHg)	154.0 (120, 192)	151.5 (90, 188)	0.922
DBP (mmHg)	93 (55, 101)	91.0 (60, 110)	0.616
TC (mmol/L)	5.08 ± 1.51	5.69 ± 1.15	0.241
TG (mmol/L)	1.24 ± 0.47	2.11 ± 1.62	0.001*
HDL-C (mmol/L)	1.85 ± 0.56	1.51 ± 0.36	0.096
LDL-C (mmol/L)	4.93 ± 2.19	4.82 ± 1.67	0.882
non-HDL-C (mmol/L)	3.23 ± 1.05	4.18 ± 1.13	0.021*
LDL-C/ HDL-C	2.66 ± 0.94	3.25 ± 1.01	0.092
TG/ HDL-C	0.73 ± 0.33	1.46 ± 1.06	0.000*
Non-HDL-C/ HDL-C	1.79 ± 0.43	2.95 ± 1.12	0.000*

[a]The t-test, Fisher's test, and the T2 test were used to compare proportions, *p < 0.05, SD - Standard deviation, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure, TC - total cholesterol, TG - triglyceride, LDL-C - low-density lipoprotein cholesterol, HDL-C - high-density lipoprotein cholesterol, Non-HDL-C - non-high-density lipoprotein cholesterol, cIMT - carotid intima-media thickness.

Table 4. Spearman rank correlations between lipid parameters, other variables and carotid intima-media thickness.

Variables	r	[a]P-value
Age (years)	0.054	0.636
Sex (male: female)	-0.137	0.233
BMI, Kg/m^2	0.014	0.900
Smoking	0.134	0.243
SBP (mmHg)	0.006	0.978
DBP (mmHg)	-0.083	0.469
TC (mmol/L)	0.346	0.002*
TG (mmol/L)	0.340	0.002*
HDL-C (mmol/L)	-0.115	0.318
LDL-C (mmol/L)	0.132	0.251
non-HDL-C (mmol/L)	0.408	0.000*
LDL-C/ HDL-C	0.270	0.017*
TG/ HDL-C	0.351	0.002*
Non-HDL-C/ HDL-C	0.369	0.001*

[a]Spearman rank correlation test, *p < 0.05, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure, TC - total cholesterol, TG - triglyceride, LDL-C - low-density lipoprotein cholesterol, HDL-C - high-density lipoprotein cholesterol.

Table 5. Associations between lipid parameters, other variables and carotid intima-media thickness.

Variables	Beta	Standard Beta	VIF	[a]P-value
Age (years)	0.003	0.066	1.000	0.564
Gender	-0.075	-0.102	1.000	0.375
BMI, kg/m^2	0.002	0.028	1.000	0.808
Smoking	-0.087	-0.115	1.000	0.318
SBP (mmHg)	0.001	0.036	1.000	0.755
DBP (mmHg)	0.001	-0.012	1.000	0.919
TC (mmol/L)	0.114	0.371	1.000	0.001*
TG (mmol/L)	0.087	0.362	1.000	0.001*
HDL-C (mmol/L)	-0.158	-0.172	1.000	0.135
LDL-C (mmol/L)	0.026	0.122	1.000	0.290
Non-HDL-C (mmol/L)	0.143	0.447	1.000	0.000*
LDL-C/ HDL-C	0.105	0.287	1.000	0.011*
TG/ HDL-C	0.142	0.391	1.000	0.000*
Non-HDL-C/ HDL-C	0.135	0.410	1.000	0.000*

[a]Univariate linear regression analysis, *p < 0.05, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure, TC - total cholesterol, TG - triglyceride, LDL-C - low-density lipoprotein cholesterol, HDL-C - high-density lipoprotein cholesterol, Non-HDL-C - non-high-density lipoprotein cholesterol, VIF - variance inflation factor.

Table 6. Predictor for carotid intima-media thickness by multiple linear regression analysis.

Variable	Beta	Standardized Beta	VIF	[a]P-value
Non-HDL-C (mmol/L)	0.266	0.434	3.069	0.042*
TC (mmol/L)	0.171	1.301	3.341	0.143
TG (mmol/L)	0.006	0.055	2.493	0.948
LDL-C/ HDL-C	0.003	0.021	2.161	0.891
TG/ HDL-C	0.009	0.137	4.229	0.949
Non-HDL-C/ HDL-C	0.061	0.431	2.875	0.518

[a]Multiple linear regression analysis, *p < 0.05, Non-HDL-C - non-high-density lipoprotein cholesterol, TC - total cholesterol, TG - triglyceride, VIF - variance inflation factor.

Table 7. Associations between lipid profiles, other variables and carotid plaque.

Variables	Beta	OR	95% CI	[a]P-value
Age (years)	-0.017	0.983	0.929 - 1.040	0.551
Gender	0.197	1.218	0.498 - 2.976	0.666
BMI, kg/m^2	0.062	0.940	0.868 - 1.018	0.128
Smoking	0.219	0.804	0.320 - 2.021	0.642
SBP (mmHg)	0.001	0.999	0.976 - 1.023	0.922
DBP (mmHg)	0.005	0.995	0.956 - 1.036	0.822
TC (mmol/L)	1.008	0.365	0.218 - 0.611	0.000*
TG (mmol/L)	1.587	0.205	0.088 - 0.478	0.000*
HDL-C (mmol/L)	-0.018	0.982	0.320 - 3.016	0.975
LDL-C (mmol/L)	0.485	0.616	0.439 - 0.863	0.005*
Non-HDL-C (mmol/L)	1.086	0.338	0.197 - 0.577	0.000*
LDL-C/ HDL-C	0.950	0.387	0.212 - 0.707	0.002*
TG/ HDL-C	1.395	0.248	0.101 - 0.609	0.002*
Non-HDL-C/ HDL-C	0.615	0.540	0.340 - 0.860	0.009*

[a]Univariate logistic regression analysis, *p < 0.05, OR - odds ratio, CI - confidence interval, BMI - body mass index, SBP - systolic blood pressure, DBP - diastolic blood pressure, TC - total cholesterol, TG - triglyceride, LDL-C - low-density lipoprotein cholesterol, HDL-C - high-density lipoprotein cholesterol, Non-HDL-C - non-high-density lipoprotein cholesterol.

Table 8. Predictors for carotid plaque by multivariate logistic regression analysis.

Variables	OR	95% CI	VIF	[a]P-value
LDL-C (mmol/L)	9.085	1.490 - 55.409	4.799	0.017*
Non-HDL-C/ HDL-C	8.335	2.984 - 23.287	3.886	0.009*
LDL-C/ HDL-C	0.021	0.001 - 0.432	4.775	0.012
Non-HDL-C (mmol/L)	0.016	0.001 - 0.215	4.015	0.002

[a]Multivariate logistic regression analysis, *p < 0.05, OR - odds ratio, CI - confidence interval, LDL-C - low-density lipoprotein cholesterol, Non-HDL-C - non-high-density lipoprotein cholesterol, VIF - variance inflation factor.

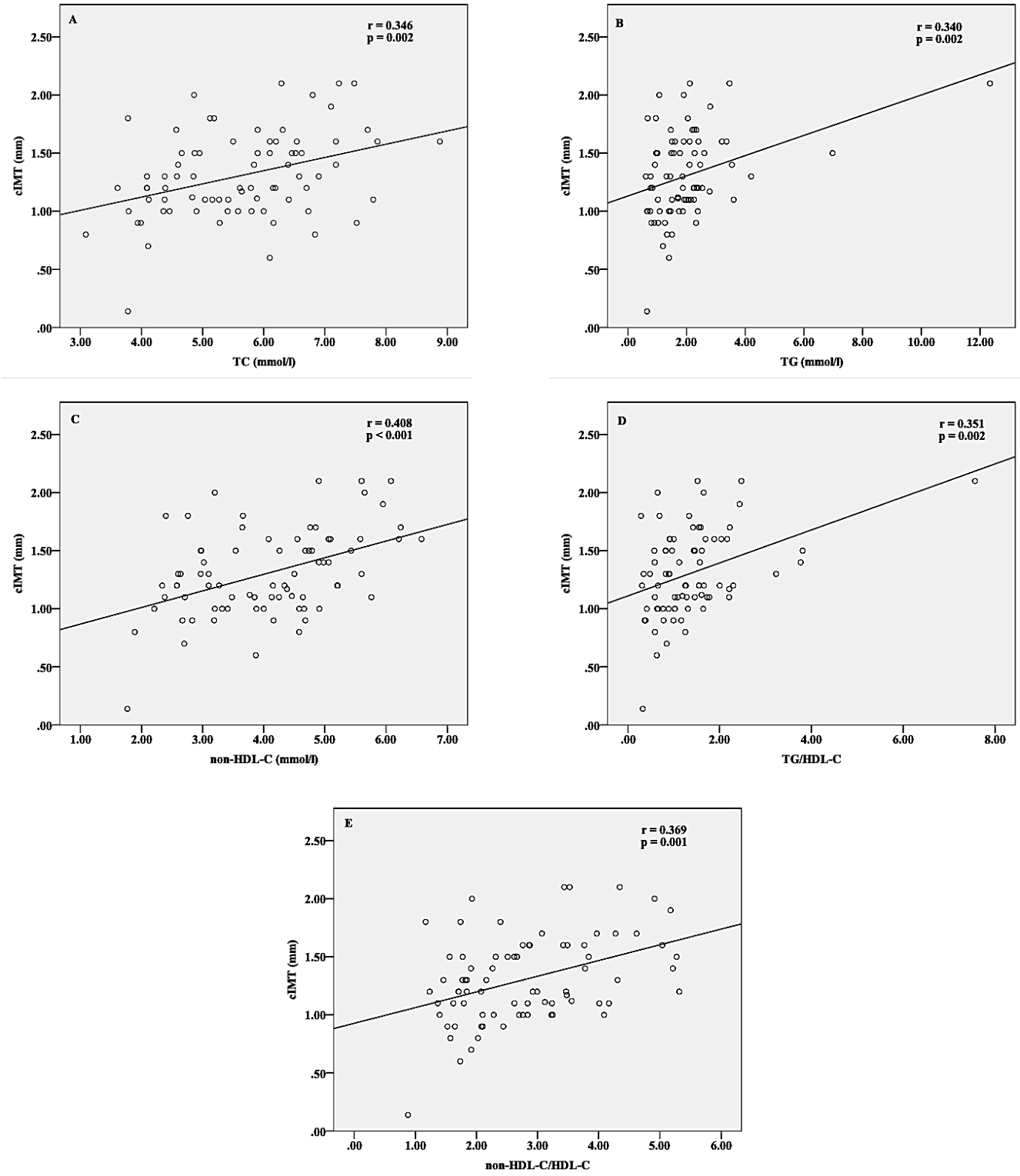

Figure 1. Correlation of carotid intima-media thickness (cIMT) with lipid profiles. T. TC - total cholesterol, B. TG - triglyceride, C. Non-HDL-C - non-high-density lipoprotein cholesterol, D. TG/HDL-C ratio, E. Non-HDL-C/HDL-C ratio

Discussion

This is the first study we are aware of to explore the association between lipids and different stages of atherosclerosis among a Mongolian population with a high stroke risk. An early manifestation of atherosclerosis was cIMT thickening, while plaque formation was a late sign of atherosclerosis. In this high-stoke-risk population, the levels of TC, TG, non-HDL-C, and TG/HDL-C, non-HDL-C/HDL-C ratios were significantly associated with the mean cIMT. High levels of non-HDL-C were an independent risk factor of early atherosclerosis. Nevertheless, an increase in LDL-C and the non-HDL-C/HDL-C ratio were associated with a higher risk of late-stage atherosclerosis.

There is evidence that LDL-C causes the development of atherosclerosis [19]. A previous study showed that LDL-C was a risk factor for any carotid plaque as well as for multiple plaques [20]. Another study explored the correlation between blood lipid profile and atherosclerosis, finding that LDL-C was positively associated with the presence of carotid plaque [21]. A large community-based cohort study suggested that elevated LDL-C was an independent predictor of carotid plaques among middle-aged German women [22]. Similar findings were observed in our study. Our results support that the level of LDL-C was a major determinant of atherosclerosis progress, and the multivariate analysis confirmed the increase in carotid plaque risk with increasing LDL-C levels in participants 55 years and older. This study supported previous results that serum LDL-C is a significant risk factor for atherosclerosis, particularly in middle-aged individuals [23]. The underlying mechanism by which LDL-C leads to arterial atherosclerosis is well established. Once the endothelial cell layer is injured, LDL-C accumulates on the arterial wall, forming fatty streaks and foam cells, both hallmarks of atherosclerotic lesions [24]. This also explains the finding that LDL affected the entire process of atherosclerosis.

Multivariate analysis demonstrated that non-HDL-C was a positive predictor for cIMT in our study, consistent with the previous findings. Previous published endemic surveys have shown that non-HDL-C is a somewhat better predictor for CVD risk than LDL-C [25, 26]. Another meta-analysis of more than 300,000 people demonstrated that the predictive value of non-HDL-C for CVD risk is not inferior to that of LDL-C (both measured and calculated) [27]. Non-HDL-C as a risk predictor of atherosclerosis has several advantages. First, it contains all potential atherogenic lipid particles; second, it can be calculated in the non-fasting state; and third, it can be calculated in the setting of hypertriglyceridemia.

We found an independent, positive relationship between the non-HDL-C/HDL-C ratio and carotid plaques. Subjects had an 8.33-fold elevated chance of having carotid plaques with a per unit increase in the non-HDL-C/HDL-C ratio, and this association was also found in most subgroups. The findings indicate that in a Mongolian population with a high risk of stroke, an increased non-HDL-C/HDL-C ratio is related to an elevated chance of having carotid plaques. Qin et al. [28] suggested that an increased non-HDL-C/HDL-C was significantly associated with elevated cIMT among Chinese individuals with metabolic syndrome. The present study provides further evidence that the non-HDL-C/HDL-C ratio positively correlated with carotid plaques. In addition, this study extends previous work on associations of the non-HDL-C/HDL-C ratio with carotid plaques from postmenopausal middle-aged females to the case of a high-stoke-risk population [29]. Markedly, the significant association between the non-HDL-C/HDL-C ratio and carotid plaques was mainly due to non-HDL-C rather than HDL-C, as HDL-C did not significantly influence our study. The findings from our study showed that an elevated non-HDL-C/HDL-C ratio was still significantly and independently related to a higher chance of having carotid plaques, providing further evidence that overall, the non-HDL-C/HDL-C ratio is a reliable parameter for evaluating carotid plaques in this high-stroke-risk population.

Previous studies presented inconsistent conclusions regarding the relationship between traditional lipid profiles and carotid plaques in different populations. A community-based study from China suggested that TC and LDL-C, but not TG, were strongly associated with CA in a general population [30]. However, several studies have previously reported that TG was also positively and significantly associated with CA in different populations [31 - 35]. In particular, a large Chinese study found that TG was independently associated with carotid plaques in a high-risk-stroke population, whereas LDL-C and TC were not significantly associated with carotid plaques [36]. Equally, findings from this study showed that LDL-C and non-HDL-C/HDL-C ratio, but not TG or HDL-C, were independently related to the presence of carotid plaques. Therefore, this issue is still controversial in the literature. Discrepancies in the population selection or sample size might cause the obvious differences

between this and previous studies.

This study has several limitations. First, it is an observational study with a relatively small sample size. Second, although the study was conducted in two centers, we cannot generalize the results to other regions or nations. A multicenter, prospective cohort study with a larger sample size or clinical trials with lipid-lowering therapy is needed for the future. Additionally, detailed further studies among selected patients with carotid atherosclerosis would be of great importance to make more generalizable conclusions in specific patient groups. Moreover, this study only identified predictors of plaque formation due to insufficient data. Quantitative characteristics of carotid plaques, such as plaque number, thickness, area, type, and Doppler ultrasound blood flow velocities, require further investigation.

Conclusions

Among the standard lipid parameters, our findings indicate that non-HDL-C was an independent risk factor for cIMT. Elevated non-HDL-C/HDL-C ratio and LDL-C level were prominently correlated with carotid plaques in the Mongolian high-stroke-risk population. A prospective randomized clinical trial of lipid-lowering therapy is needed to assess the causal nature of the relationship among the Mongolian people.

Conflict of Interest

The authors declare no conflict of interest.

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