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Differential effects of hyperhomocysteinemia on the lipid profiles and lipid ratios between patients with and without coronary artery disease

A retrospective observational study

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Abstract

This study aimed to investigate the differential effects of hyperhomocysteinemia (HHcy) on lipid profiles and lipid ratios between patients with coronary artery disease (CAD) and without CAD. The data of 872 CAD patients and 774 non-CAD controls were extracted from the information system of hospitalized patients. Serum homocysteine (Hcy), total cholesterol (TC), triglycerides (TGs), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein (Apo) AI, and ApoB concentrations were detected. HHcy was defined as a serum level of Hcy ≥ 15 μmol/L. The CAD patients had lower levels of HDL-C and ApoAI and higher levels of Hcy than the controls ($P < .05$). Serum TGs and HDL-C were negatively correlated with Hcy in controls. Serum HDL-C and ApoAI were negatively correlated with Hcy, and the ratios of TC/HDL-C, TG/HDL-C, LDL/HDL-C, and ApoB/ApoAI were positively correlated with Hcy in the CAD patients ($P < .05$). Although the trends for HHcy to decrease the lipid profiles were not different between the CAD and controls (*Pinteraction* > 0.05), CAD with HHcy had lower HDL-C and ApoAI levels than those of subjects with normal Hcy; controls with HHcy had lower TC, LDL-C, and ApoB levels than those of subjects with normal Hcy ($P < .05$). There were different HHcy trends affecting the ratios of TC/HDL-C and LDL/HDL-C between the CAD patients and controls (*Pinteraction* for TC/HDL-C = 0.025; *Pinteraction* for LDL/HDL-C = 0.033). CAD patients with HHcy had a higher ratio of TC/HDL-C ($P = .022$) and LDL/HDL-C ($P = .045$) than those of patients with normal Hcy, but in the controls, the subjects with HHcy exhibited a trend toward a decreased ratio of TC/HDL-C ($P = .481$) and LDL/HDL-C ($P = .303$). There were differential effects of HHcy on the lipid ratios between CAD and non-CAD patients. HHcy was related to higher ratios of TC/HDL-C and LDL/HDL-C in patients with CAD.

Abbreviations: Apo = apolipoprotein, CAD = coronary artery disease, CVD = cardiovascular disease, Hcy = homocysteine, HDL-C = high-density lipoprotein cholesterol, HHcy = hyperhomocysteinemia, LDL-C = low-density lipoprotein cholesterol, MTHFR = methylene tetrahydrofolate reductase, NF-Kb = Nuclear factor κB, TC = total cholesterol, TG = triglycerides, VLDL-C = very low-density lipoprotein cholesterol.

Keywords: Coronary artery disease, hyperhomocysteinemia, lipid ratios, serum lipid level

1. Introduction

Coronary artery disease (CAD) is the leading cause of death worldwide and remains a major health problem in both developed and developing countries.[1] Traditional lipid parameters, such as increased serum levels of total cholesterol (TC), triglycerides (TGs), low-density lipoprotein cholesterol (LDL-C), and apolipoprotein (Apo) B or low levels of high-density lipoprotein cholesterol (HDL-C) and ApoAI, are among the most important modifiable risk factors for CAD.[2,3] It has also been reported that nontraditional lipid profiles (lipid ratios) are a powerful predictor of cardiovascular disease (CVD).[4–8] For instance, after a 10-year follow-up of a prospective cohort study including 15,632 initially healthy US women, it was suggested that the TC/HDL-C ratio was as good as or better than apolipoprotein fractions for the prediction of future cardiovascular

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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events.[6] Moreover, the LDL-C/HDL-C ratio has been found to be an independent indicator of vascular risk with greater predictive value than isolated lipid levels.[8]

Despite therapeutic advances that control many risk factors, such as statins that have decreased LDL-C levels to lower levels than previously possible, CVD remains a major cause of morbidity and mortality worldwide.[9] Hyperhomocysteinemia (HHcy) has been regarded as a potential new risk factor for CVD. HHcy acts through various mechanisms, including vascular endothelial damage, stimulation of smooth muscle cell proliferation, and thrombosis activation.[10,11] Previous studies have shown that HHcy and serum Hcy are positively correlated with serum TC, LDL-C, and TG levels[12,13] and negatively correlated with serum HDL-C[12–17] and ApoAI[17] levels in physical examination populations or community-based populations. However, the VLDL-21 study[18] failed to find an association between HHcy and lipid profiles in a large population. In patients with diagnosed CAD, serum Hcy was positively correlated with LDL-C[19] and TGs[20] and negatively correlated with HDL-C[19–21] and ApoAI.[21] Conversely, Kiseljaković et al[22] observed a negative association between serum Hcy and TC, LDL-C and very-low-density lipoprotein cholesterol (VLDL-C) in atherosclerotic vascular disease patients with HHcy.

Among the above studies, the research results on the relationship between HHcy and blood lipid levels are inconsistent, and there may be differences in this relationship between CAD and non-CAD. To date, there have been limited epidemic data concerning the relationship between HHcy and lipid ratios and the differential effects of HHcy on the lipid profiles between CAD and non-CAD participants. Thus, the present study aimed to investigate the differential effects of HHcy on the lipid profiles and lipid ratios between patients with CAD and patients without CAD.

2. Materials and methods

2.1. Subjects

The data of 872 diagnosed CAD patients and 774 non-CAD controls were extracted from the information system of hospitalized patients in Guangxi Academy of Medical Sciences and the People's Hospital of Guangxi Zhuang Autonomous Region. As described in detail in a previous study,[23] the diagnosis of CAD is mainly based on the results of coronary angiography. CAD was defined as significant coronary stenosis (≥ 50%) in at least one of the 3 main coronary arteries or their major branches (branch diameter ≥ 2 mm). The inclusion criteria of the non-CAD controls were that coronary angiography showed no obvious coronary stenosis, and there was no clinical evidence of acute coronary syndrome based on troponin detection and electrocardiogram. In the CAD and control groups, patients with congenital heart disease, cardiomyopathy, valvular disease, autoimmune disease, or type I diabetes mellitus were excluded. The study protocol was approved by the Ethics Committee of Guangxi Academy of Medical Sciences and the People's Hospital of Guangxi Zhuang Autonomous Region. Informed consent was obtained from all subjects after they had received a full explanation of the study.

2.2. Blood sample collection and laboratory methods

After an overnight fast of at least 12 hours, a venous blood sample was obtained from the forearm of each patient, as described in detail in our previous study.[24] Serum Hcy was measured using an enzymatic cycling method. Serum TC, LDL-C, HDL-C, and TGs were measured by enzymatic methods with commercially available kits on a Beckman Coulter Automatic Analyzer. Serum ApoAI and ApoB levels were detected by immunoturbidimetric immunoassays. All of these biochemical analyses were performed at the Clinical Laboratory of Guangxi Academy of Medical Sciences and the People's Hospital of Guangxi Zhuang Autonomous Region. According to the results from previous studies,[24] Hcy ≥ 15 μmol/L is often defined as HHcy.

2.3. Statistical analyses

The statistical software package SPSS 22.0 (SPSS Inc., Chicago, IL) was used for the statistical analyses. Quantitative variables are expressed as the mean ± standard deviation. Qualitative variables are expressed as raw counts and percentages. The differences in the general characteristics between patients and controls were tested by Student's unpaired *t* test or chi-square analysis. Comparison of blood lipid parameters between the different groups was performed by analysis of covariance (ANCOVA). Multivariate linear regression analysis with stepwise modeling was performed to evaluate the association of serum Hcy levels with serum lipid levels and lipid ratios. Sex, age, body mass index, diabetes, and hypertension were adjusted for in the statistical analysis. A 2-tailed *P* value of less than .05 was considered statistically significant.

3. Results

3.1. General characteristics and serum lipid levels in CAD patients and non-CAD controls

Table 1 shows the general characteristics and serum lipid parameters of the study population. Compared with the proportions in the controls, the CAD patients had a higher proportion of

Table 1

General characteristics and serum Hcy levels in CAD patients and controls.

Parameters	Controls	CAD	*t/x2*	*P*
N	774	872	–	–
Age	63.66 ± 29.81	63.27 ± 10.40	0.362	0.730
Male/Female	432/342	634/238	51.273	0.000
Hypertension	198(25.6)	269(30.8)	5.598	0.018
Diabetes	88(11.4)	106(12.2)	0.244	0.621
TC (mmol/L)	4.53 ± 1.13	4.44 ± 1.22	1.654	0.097
TG (mmol/L)	1.56 ± 0.95	1.66 ± 1.12	-1.940	0.053
HDL-C (mmol/L)	1.15 ± 0.30	1.11 ± 0.32	2.467	0.014
LDL-C (mmol/L)	2.74 ± 0.80	2.66 ± 0.98	1.810	0.071
ApoAI (g/L)	1.18 ± 0.26	1.07 ± 0.31	7.350	0.000
ApoB (g/L)	0.91 ± 0.25	0.90 ± 0.29	0.277	0.780
Hcy (umol/l)	13.50 ± 5.84	15.11 ± 5.20	-5.928	0.000

ApoAI = apolipoprotein AI, ApoB = apolipoprotein B, CAD = coronary artery disease, Hcy = homocysteine, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

males and individuals with hypertension, lower levels of HDL-C and ApoAI, and a higher level of serum Hcy (P for all < 0.05). Perhaps due to the effects of lipid-lowering drugs, there were no significant differences in the levels of serum TC, TGs, LDL-C, or ApoB; there were also no significant differences in the age distribution or the prevalence of diabetes between the 2 groups (P > .05 for all).

3.2. Correlation of Hcy and serum lipid parameters in CAD patients and non-CAD controls

The correlation between Hcy and serum lipid parameters is shown in Table 2. Sex, age, body mass index, diabetes, and hypertension were excluded from the statistical analysis. Multiple linear regression analysis showed that serum TGs and HDL-C were negatively correlated with Hcy in controls. In CAD patients, serum HDL-C and ApoAI were negatively correlated with Hcy, and the ratios of TC/HDL-C, TG/HDL-C, LDL/HDL-C, and ApoB/ApoAI were positively correlated with Hcy (P < .05 for each).

3.3. HHcy and serum lipid levels in CAD patients and non-CAD controls

As shown in Table 3, when statistical analysis was performed between the normal Hcy and HHcy groups according to whether the serum Hcy concentration was greater than 15 μmol/L, CAD subjects with HHcy had lower HDL-C and ApoAI levels than subjects with normal Hcy; control subjects with HHcy had lower TC, LDL-C, and ApoB levels than subjects with normal Hcy (P for all < 0.05). There were no significant interactions between HHcy and disease in terms of serum lipid levels ($P_{interaction}$ for all > 0.05).

3.4. HHcy and lipid ratios in CAD patients and non-CAD controls

As shown in Table 4 and Fig. 1, there were different trends in the effects of HHcy on the ratios of TC/HDL-C and LDL-C/HDL-C between the CAD patients and controls ($P_{interaction}$ for TC/HDL-C = 0.025; $P_{interaction}$ for LDL-C/HDL-C = 0.033). CAD patients with HHcy had a significantly higher ratio of TC/HDL-C than patients with normal Hcy (normal Hcy: 4.10 ± 1.32 vs HHcy: 4.43 ± 2.60, P = .025), but in the controls, the subjects with HHcy exhibited a trend toward a decreased ratio of TC/HDL-C (normal Hcy: 4.11 ± 1.03 vs HHcy: 4.05 ± 1.11, P = .481). CAD patients with HHcy had a higher ratio of LDL/HDL-C (normal Hcy: 2.48 ± 1.07 vs HHcy: 2.65 ± 1.36; P = .045), but in the controls, the subjects with HHcy exhibited a trend toward a decreased ratio of LDL/HDL-C (normal Hcy: 2.52 ± 0.80 vs HHcy: 2.45 ± 0.85; P = .303).

4. Discussion

CAD is one of the leading causes of morbidity and mortality worldwide. Despite clinicians' best efforts, available therapies protect only 30 and 40% of individuals at risk.[9] Thus, it is important to investigate new predictors of CAD to help protect against and provide a new treatment for CAD. A possible relationship between HHcy and CAD was first suggested by Wilcken et al in 1976.[25] Since then, more data from various epidemiological investigations and laboratory studies have demonstrated that an increased concentration of serum Hcy was considered to be an independent risk factor for CVD. A meta-analysis showed that an increase of 5 μmol/L in plasma Hcy levels enhances the risk of CVD by 1.6- to 1.8-fold, which is similar to the risk seen with an increase of 20 mg/dL (0.52 mmol/L) in cholesterol concentration.[26] The causes of HHcy are multifactorial, but folate, vitamin B6, and B12 deficiencies are the main causes of HHcy.[27] Methylene tetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism, and the genetic variation of the C677TT genotype is also related to increased Hcy levels, and increased risk of CAD.[28] The possible mechanisms of elevated Hcy that lead to the development and progression of vascular disease include effects on platelets, clotting factors, the endothelium, and thrombosis.[27,29] Although an increased intake of fruits and vegetables and supplementation with folic acid and B vitamins can lower Hcy safely and inexpensively, and lowering Hcy levels in this manner may slow the progression of atherosclerosis in coronary and carotid vessels in some studies,[30] supplements combining folic acid and vitamins B6 and B12 did not reduce the risk of major cardiovascular events in patients with vascular disease in a randomized controlled trial study.[31] Therefore, clinical and basic studies on the role of Hcy in vascular diseases remain to be further explored. In this study, we also found that serum Hcy was higher in CAD patients, which verified the positive correlation between Hcy levels and CAD in our study. It is well known that serum lipid levels are the most important risk factors for CAD. In the present study, serum HDL-C and ApoAI were lower in CAD patients, suggesting a negative correlation between HDL-C and ApoAI levels and CAD in our study. Therefore, we speculate that serum Hcy may correlate with the blood lipid profile, especially HDL-C and ApoAI. Multiple linear regression analysis showed that serum TGs and HDL-C were negatively correlated with Hcy in controls. Serum HDL-C and ApoAI were negatively correlated with Hcy in CAD, and the ratios of TC/HDL-C, TG/HDL-C, LDL/HDL-C, and ApoB/ApoAI were positively correlated with Hcy only in CAD patients but not in controls. This finding also suggests that there were differences in the relationship of HHcy

Table 2

Correlation of Hcy with serum lipid parameters and lipid ratios in CAD patients and controls.

Relative factor	Unstandardized coefficient	Std. error	Standardized coefficient	*t*	*P*
Control					
TG	–0.616	0.223	–0.100	–2.768	0.006
HDL-C	–1.614	0.706	–0.083	–2.287	0.022
CAD					
HDL-C	–1.499	0.624	–0.092	–2.404	0.016
ApoAI	–1.652	0.668	–0.095	–2.473	0.014
TC/HDL-C	0.200	0.084	0.078	2.375	0.018
TG/HDL-C	0.234	0.099	0.078	2.360	0.019
LDL/HDL-C	0.400	0.143	0.093	2.802	0.005
ApoB/ApoAI	1.415	0.498	0.096	2.840	0.005

ApoAI = apolipoprotein AI, ApoB = apolipoprotein B, CAD = coronary artery disease, Hcy = homocysteine, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

Table 3

HHcy and serum lipid levels in CAD patients and controls.

Group	N	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoAI (g/L)	ApoB (g/L)
Control							
Normal Hcy	532	4.60 ± 1.20	1.61 ± 0.99	1.16 ± 0.31	2.80 ± 0.83	1.19 ± 0.26	0.92 ± 0.26
HHcy	242	4.37 ± 0.94	1.46 ± 0.83	1.13 ± 0.27	2.61 ± 0.66	1.16 ± 0.24	0.88 ± 0.21
F		6.856	3.677	1.827	9.039	2.119	5.013
P		0.009	0.056	0.177	0.003	0.146	0.025
CAD							
Normal Hcy	484	4.49 ± 1.32	1.69 ± 1.20	1.15 ± 0.30	2.70 ± 1.05	1.10 ± 0.25	0.91 ± 0.31
HHcy	388	4.37 ± 1.06	1.63 ± 1.01	1.07 ± 0.34	2.62 ± 0.86	1.04 ± 0.37	0.89 ± 0.25
F		1.783	0.525	10.202	1.279	6.197	0.650
P		0.182	0.469	0.001	0.258	0.013	0.420
*P*interaction		0.303	0.615	0.382	0.240	0.667	0.363

ApoAI = apolipoprotein AI, ApoB = apolipoprotein B, CAD = coronary artery disease, Hcy = homocysteine, HDL-C = high-density lipoprotein cholesterol, HHcy = hyperhomocysteinemia, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

Table 4

Lipid ratios in the HHcy and normal Hcy groups.

Group	N	TC/HDL-C	TG/HDL-C	LDL/HDL-C	ApoB/ApoAI
Control					
Normal Hcy	532	4.11 ± 1.03	1.50 ± 1.02	2.52 ± 0.80	0.80 ± 0.27
HHcy	242	4.05 ± 1.11	1.43 ± 1.00	2.45 ± 0.85	0.79 ± 0.27
F		0.498	0.781	1.063	0.210
P		0.481	0.377	0.303	0.647
CAD					
Normal Hcy	484	4.10 ± 1.32	1.60 ± 1.27	2.48 ± 1.07	0.87 ± 0.35
HHcy	388	4.43 ± 2.60	1.79 ± 2.18	2.65 ± 1.36	0.92 ± 0.36
F		5.276	2.431	3.860	4.372
P		0.022	0.119	0.045	0.037
*P*interaction		0.025	0.144	0.033	0.094

ApoAI = apolipoprotein AI, ApoB = apolipoprotein B, CAD = coronary artery disease, Hcy = homocysteine, HDL-C = high-density lipoprotein cholesterol, HHcy = hyperhomocysteinemia, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

and lipid profiles between CAD and non-CAD controls. To date, there have been limited epidemiological data concerning this point.

Statistical analysis was performed between the normal Hcy and HHcy groups according to whether the serum Hcy concentration was greater than 15 μmol/L. There were no significant differences in the trends of HHcy affecting serum lipid levels between the CAD patients and non-CAD controls. The data show that HHcy was associated with a consistently decreasing trend in all blood lipid parameters in CAD patients and non-CAD controls; however, CAD subjects with HHcy had significantly lower HDL-C and ApoAI levels than subjects with normal Hcy, and control subjects with HHcy had significantly lower TC, LDL-C and ApoB levels than subjects with normal Hcy. There were also some invaluable clinical observations that demonstrated the possible link between Hcy and lipid metabolism pathways. Consistent research findings suggest that Hcy is significantly and negatively correlated with HDL-C and ApoAI in community-based or health physical examination populations,[12–17] and these correlations also exist in patients with diagnosed CAD.[19–21] It is well known that HDL and ApoAI exert antiatherogenic effects by transporting cholesterol from cells into peripheral tissues,[32] reducing oxidative stress and suppressing inflammatory pathways.[33] Hcy promotes atherosclerotic effects through vascular endothelial damage, smooth muscle cell proliferation stimulation, and thrombosis activation.[10,11] Some studies have described the mechanism of the inverse correlation between Hcy and HDL-C or ApoAI. Mikael et al[34] demonstrated that MTHFR-deficient mice showed decreased levels of ApoAI mRNA in the liver and decreased ApoAI protein in the liver and plasma compared with MTHFR(+/+) mice. Further in vitro experiments suggested that Hcy suppresses hepatic ApoAI expression via the peroxisome proliferator-activated receptor α pathway. Moreover, HHcy inhibits reverse cholesterol transport by reducing circulating HDL by inhibiting apoA-I protein synthesis and enhancing HDL-C clearance.[35] The results of HHcy were related to decreased levels of HDL-C and ApoAI in the present study and were consistent with previous literature, which suggests that Hcy-induced HDL-C and apoA-I inhibition represent a novel mechanism by which Hcy induces atherosclerotic CVD.[36]

The associations between Hcy and serum TC, TGs and LDL-C have been explored in some clinical observation studies. Durdi et al[19] reported that in 126 myocardial infarction patients, Hcy was positively correlated with LDL-C levels. In 300 Indian subjects with proven CAD, Hcy was found to be positively associated with TGs and VLDL-C.[20] There are also 2 community-based studies that incorporated large samples in China; Momin M et al[16] showed that HHcy was independently associated with hypertriglyceridemia, and Qin YY et al[13] showed that HHcy was related to high concentrations of TC, TGs, and LDL-C. These results suggest that HHcy is related to the risk factors for promoting atherosclerosis. However, 2 small sample studies found no significant correlations between HHcy and lipid profiles.[37,38] In addition, the data including 18,297 US adults from the very large database of lipids (VLDL-21) showed inconsistent results. In unadjusted analyses, the levels of LDL-C and non-HDL-C were lower, whereas the levels of TGs and VLDL-C were higher in the highest Hcy quartile.[18] Similar to the VLDL-21 study, in the present study, we found that the levels of serum TC, LDL-C, and ApoB in the HHcy group were significantly lower than those in the normal Hcy group in non-CAD controls, which contrasts with most previous studies[13,16,19,20] and appears to suggest that HHcy is associated

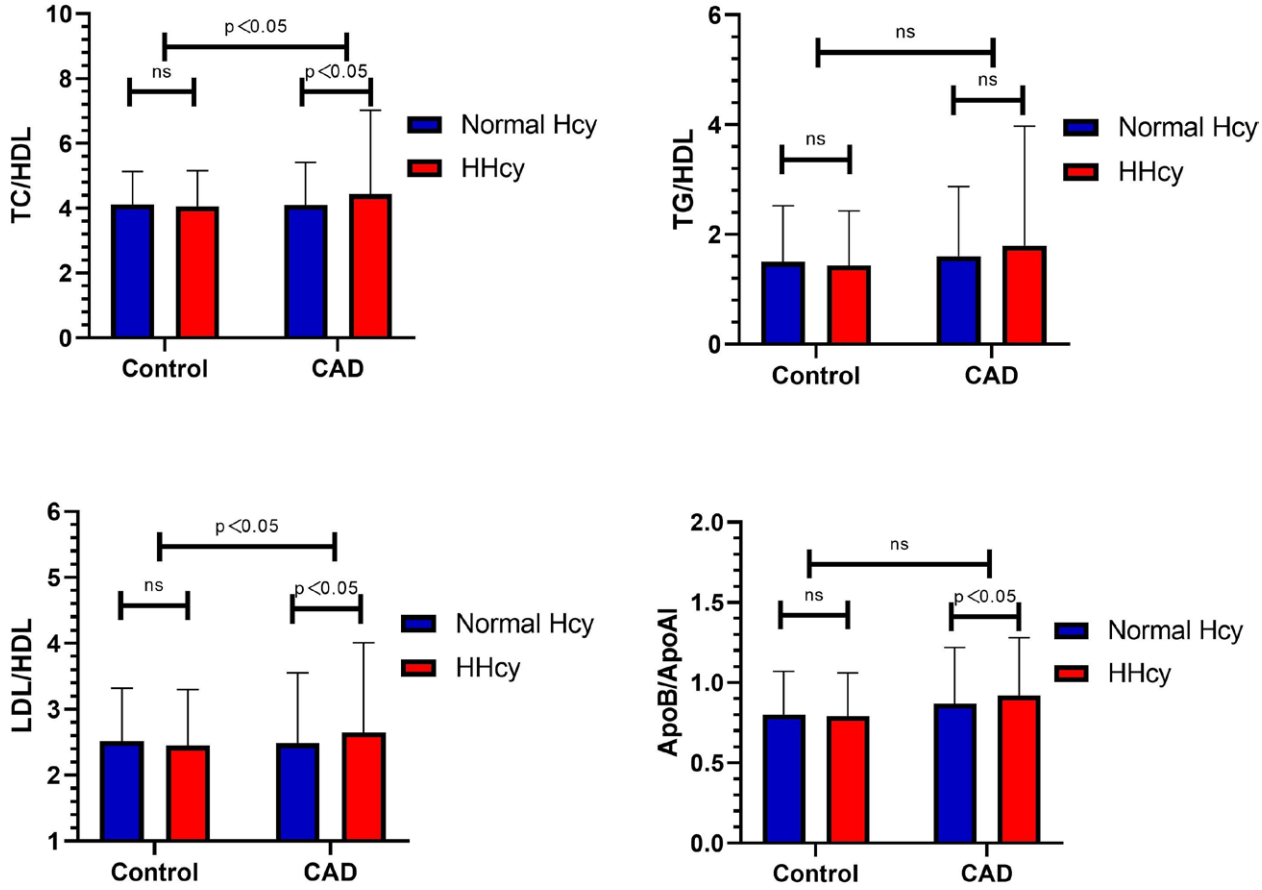

Figure 1. Lipid ratios in the HHcy and normal Hcy groups. Hcy = homocysteine, HHcy = hyperhomocysteinemia.

with lipid parameters in the protection against atherosclerosis in these populations. To explain these contradictions, it must be noted that information on lipid-lowering medication, one of the most important confounders, was unknown in our non-CAD controls and the VLDL-21 study. In a previous study, we showed that the change in blood lipid levels after atorvastatin treatment was regulated by the change in Hcy levels,[24] which suggested that the relationship between Hcy and blood lipid levels may also be affected by statins; however, in the present observational study, we lacked complete information about who took statins, the dose, the treatment course of lipid-lowering drugs and the baseline lipid level before treatment. Further research is needed to clarify the effect of the interaction between HHcy and lipid-lowering drugs on blood lipids. Therefore, it is difficult to determine whether HHcy promotes atherosclerosis or protects against atherosclerosis by evaluating indicators such as TC, LDL, and ApoB.

Nontraditional lipid profiles, including TC/HDL-C, LDL/HDL-C, TG/HDL-C, and ApoB/ApoAI, have been found to be independent indicators of vascular risk with greater predictive value than isolated lipid levels.[4–8] Therefore, the blood lipid ratio is very useful for clarifying whether HHcy is associated with promoting atherosclerosis or protecting against atherosclerotic lipid profiles. At present, no study has observed the effect of HHcy on blood lipid ratios or the differential effect between CAD patients and non-CAD patients. The present study showed that different trends in HHcy affect the ratio of TC/HDL-C and LDL-C/HDL-C between the CAD and non-CAD controls (P for interaction < 0.05). In the controls, HHcy was associated with a decreasing trend in the ratio of TC/HDL-C (normal Hcy: 4.11 ± 1.03 vs HHcy: 4.05 ± 1.11; P = .481) and LDL/HDL-C (normal Hcy: 2.52 ± 0.80 vs HHcy: 2.45 ± 0.85; P = .303); however, CAD patients with HHcy had a significantly higher ratio of TC/HDL-C (normal Hcy: 4.10 ± 1.32 vs HHcy: 4.43 ± 2.60; P = .025) and a higher LDL/HDL-C ratio (normal Hcy: 2.48 ± 1.07 vs HHcy: 2.65 ± 1.36; P = .045) than normal Hcy patients. The importance of TC/HDL-C and LDL/HDL-C in predicting cardiovascular events was highlighted in some large studies. Ridker et al[6] showed that the use of the ratio of TC/HDL-C was as good as or better than apolipoprotein fractions in the prediction of future cardiovascular events. Arsenault et al[39] observed that at any LDL-C level, individuals with an elevated TC/HDL-C ratio were still at an increased risk of developing CAD. The PROSPER trial,[40] a retrospective analysis of 6000 patients, found that the LDL-C/HDL-C ratio was the most powerful measure of CVD risk in elderly people, and the changes in the LDL-C/HDL-C ratio as a result of statin treatment appeared to account for the beneficial effects of therapy. Therefore, in people taking lipid-lowering drugs, the ratio of blood lipids is more suitable for assessing the effect of HHcy on CAD risk. Not surprisingly, HHcy is related to the atherogenic lipid profile because it increases the ratio of TC/HDL-C and LDL/HDL-C; however, the present findings also suggest that HHcy plays a more important role in the atherogenic lipid profile of CAD patients than that of subjects without CAD. Although the possible reasons for the disease-specific relationship between the effect of HHcy on the blood lipid ratio have not been clarified, some possible explanations are that there were different cardiovascular risk factors, different baseline blood lipid levels[41] and different drug effects[42] between CAD patients and non-CAD patients, which may partly explain the differential effects of HHcy on the lipid ratios between CAD patients and non-CAD controls. Further research should be carried out to clarify this disease-specific relationship.

5. Conclusion

There were differential effects of HHcy on the lipid ratios between CAD patients and non-CAD controls. HHcy was related to a higher ratio of TC/HDL-C and LDL/HDL-C in patients with CAD. The ratio of blood lipids should be given more attention to assess the effect of HHcy on CAD risk.

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