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# Gender specific effect of *CETP* rs708272 polymorphism on lipid and atherogenic index of plasma levels but not on the risk of coronary artery disease

## A case–control study

Gaojun Cai, MM[a,*], Ganwei Shi, MM[a], Zhiying Huang, MM[b]

**Abstract**

Numerous studies have shown a relationship between cholesteryl ester transfer protein (*CETP*) polymorphism in the synthesis of high-density lipoprotein cholesterol (HDL-C) and the coronary artery disease (CAD) susceptibility, but the results have remained inconsistent. In addition, there was no study exploring the relationship between *CETP* polymorphisms and atherogenic index of plasma (AIP) levels.

We conducted a case-control study to evaluate the relationship between *CETP* rs708272 polymorphism and CAD risk and lipid levels in Chinese Han population. 556 CAD patients and 414 controls undergoing coronary angiography were consecutively enrolled in the hospital-based study. Polymerase chain reaction-ligase detection reaction (PCR-LDR) method was used to detect the different genotypes at rs708272.

No significant association between *CETP* rs708272 polymorphism and CAD risk was observed in different genetic models. In the whole population, participants with TT genotype had higher HDL-C levels (1.17 ± 0.31 mmol/L vs 1.09 ± 0.29 mmol/L, $P = .001$) and lower AIP levels (0.08 ± 0.35 vs 0.16 ± 0.31, $P = .004$) compared to those with CC genotype, after adjusting for age, gender, smoking, essential hypertension (EH), and DM. The T allele carriers had higher HDL-C levels than the T allele non-carriers (1.13 ± 0.29 mmol/L vs 1.09 ± 0.29 mmol/L, $P = .023$). Furthermore, subgroup analyses based on gender were carried out. In males, the results showed that participants with TT genotype had significant higher HDL-C levels and lower AIP levels compared with CC genotype ($P < .05$). In addition, males with CT+TT genotypes had higher HDL-C levels and lower AIP levels than those with CC genotypes (HDL-C: CT+TT 1.11 ± 0.31vs CC 1.06 ± 0.30 mmol/L, $P = .041$; AIP: CT+TT 0.12 ± 0.32vs CC 0.16 ± 0.31, $P = .034$, respectively). However, there were no significant associations between lipid levels and *CETP* rs708272 polymorphism in females, after adjusting for confounders.

*CETP* rs708272 polymorphism has a gender-specific effect on lipid and AIP levels but not on the risk of CAD.

**Abbreviations:** AI = atherosclerosis index, AIP = atherogenic index of plasma, CAD = coronary artery disease, CAG = coronary angiography, CETP = cholesteryl ester transfer protein, DM = diabetes mellitus, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

**Keywords:** atherogenic index of plasma, coronary artery disease, dyslipidemia, gene, lipids, polymorphism

## 1. Introduction

Coronary artery disease (CAD) remains the serious public health problem worldwide.[1] It is well established that environmental risk factors are contributing to the development of CAD, such as smoking, essential hypertension (EH), diabetes mellitus (DM), air pollution, hyperuricemia, and dyslipidemia.[2–4] Numerous studies have concluded that high-density lipoprotein cholesterol (HDL-C), which is affected by environmental and genetic factors, is a protective factor against CAD.[5,6] However, the results were inconsistent. For example, no incremental clinic benefit was obtained from the addition of niacin to statin therapy, despite a significant increase in HDL-C levels.[7] In comparison to conventional lipid levels, comprehensive lipid index, such as atherogenic index of plasma (AIP) and atherosclerosis index (AI), could comprehensively reflect the balance between atherogenic and anti-atherogenic factors and might be a strong marker for predicting the risk of CAD and CAD-related diseases.[8,9]

The cholesteryl ester transfer protein (CETP), a hydrophobic glycoprotein, plays an important role in reverse cholesterol transport through mediating the transfer of the cholesteryl esters and triglycerides (TGs) from HDL to low-density lipoprotein (LDL) and to very-low-density lipoprotein (VLDL), which might be associated with the risk of CAD.[10] Overexpression of CETP might contribute to the development of atherosclerosis by

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*GC and GS contributed equally.*

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*[a] Department of Cardiology, Wujin Hospital affiliated with Jiangsu University, [b] Department of Pediatrics, No. 2 Hospital of Changzhou, Changzhou, Jiangsu, China.*

*[*] Correspondence: Gaojun Cai, Wujin Hospital Affiliated with Jiangsu University, Jiangsu China (e-mail: cgj982@126.com).*

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decreasing serum HDL-C levels and increasing the accumulation of macrophage-derived foam cells in lesions.[11] In addition, baseline CETP levels might predict the lipid-reducing effects of statin.[12] CETP inhibitors could increase the serum HDL-C levels and reduce the incidence of diabetes.[13] Although the effects on clinical cardiovascular outcomes had not been confirmed, several studies suggested that CETP inhibitors could reduce the risk of having a coronary event in high-risk, statin-treated patients.[14,15]

The *CETP* gene is located on 16q12-21 and encompasses16 exons and 15 introns encoding 476 amino acids.[16]*CETP* variant had a strong impact on the expression of CETP and the HDL-C levels and was associated with the lipid-regulating response to statins.[17] In a meta-analysis of genome-wide association studies (GWAS) to identify variants with an effect on HDL-C response to statins in individuals of European descent, the minor allele of *CETP* polymorphism was associated with the greater HDL-C response to statin treatment.[18] GWAS had identified some important loci in *CETP* gene that were associated with CAD and serum lipid levels. One of the most investigated variants in *CETP* gene was rs708272 (TaqIB). This variant might affect the levels and/or activity of plasma CETP, which might affect the concentrations of HDL-C.[16] Recently, numerous studies have shown a relationship between *CETP* rs708272 polymorphism in the synthesis of HDL-C and the ischemic cardiovascular disease susceptibility, but the results have remained inconsistent.[19,20] In addition, there was no study exploring the relationship between *CETP* polymorphisms and comprehensive lipid index. We conducted this hospital-based case-control study to investigate the effects of *CETP* rs708272 polymorphism on lipid and AIP levels and CAD risk in a Chinese population.

## 2. Materials and methods

### 2.1. Study subjects

A total of 556 randomly selected patients with CAD (391 males and 165 females, mean age 64.24 ± 9.94 years) and 414 control subjects (214 males and 200 females, mean age 61.49 ± 9.11 years) were recruited from the Department of Cardiology in Wujin hospital affiliated to Jiangsu University from September 2012 to July 2017. All patients had undergone coronary angiography (CAG) examination. The image was read by 2 experienced cardiologists. The diagnoses of CAD, EH, and DM were described in our previous study.[21] The controls were who had angina-like chest pain and underwent CAG examination in the same period. According to the results of CAG, controls had a luminal stenosis of <50% in the major coronary arteries. Subjects with advanced liver or kidney failure, apparent thyroid disease, malignant tumors, major surgery or trauma within 1 month, undergoing statin treatment, were excluded. Informed consent was obtained from all enrolled subjects. The study was approved by the ethics committee of our hospital.

### 2.2. Biochemical parameter analysis

Approximately 2 mL of venous blood was extracted from each participant after 12 hours fasting. Biochemical parameters, including total cholesterol (TC), TG, HDL-C, low-density lipoprotein cholesterol (LDL-C), ApoA1, ApoB and Lp(a), were analyzed by automatic biochemical analyzer (Olympus AU5400). AI is calculated as non-HLD-C/HDL-C and AIP as $\log_{10}$(TG/HDL-C).[22,23]

### 2.3. Genotyping of CETP rs708272 polymorphism

Genomic DNA was extracted from peripheral blood leukocytes and was stored at -80°C. The method of extraction was described in previous study.[24] Polymerase chain reaction and ligase detection reactions (PCR-LDR) method was performed to identify the genotypes. The total PCR reaction system was 20 μL, including 1 μL genomic DNA, 2 μL buffer, 0.6 μL $Mg2^+$, 2 μL dNTP, 0.2 μL Taq DNA polymerase, 2 μL Primer mix (forward: 5'- CCC CTG ACT CAA CCC CCT AA-3'; reverse: 5'-CCT CGC CTT CAA GGT CAA GT-3'), and 12.2 μL $ddH_2O$. The PCR reaction conditions were: a pre-degeneration at 95°C for 2 minutes, followed by 40 cycles of 94°C for 90 seconds, 53°C for 90 seconds and 65°C for 30 seconds, with a terminal extension step at 65°C for 10 minutes. After PCR amplification, the connection reaction was performed. LDR was performed with a volume of 10 μL comprising 4 μL PCR product, 1 μL buffer, 1 μL probe mix (each) (2pmol/uL) (Probe information lists in Supplement Table 1, http://links.lww.com/MD/C676), 0.05 μL Taq DNA ligase, and double distilled water up to 10 μL. LDR reaction conditions were pre-degeneration at 95°C for 2 minutes, followed by 40 cycles of 94°C for 15 seconds, and 50°C for 25 seconds. The genotypes were identified by the ABI PRISM3730 sequencer, and data were analyzed by using Genemapper software. In order to verify the accuracy of the results, a part of PCR products was randomly selected and sent to sequencing (Sangon, Shanghai).

### 2.4. Statistical analysis

The normality of the data distribution was assessed with the Kolmogorov–Smirnov test and PPlot. Continuous variables were represented as means ± standard deviation (SD) and compared with independent-sample *t* tests. Because the distribution of serum TG was highly skewed, it was represented as median [quartile ranges (QR)] and was compared using methods of Mann–Whitney *U* or Kruskal–Wallis *H* test. Qualitative variables were reported as frequency (percentage) and evaluated by Chi-square test. The genotype distribution for the Hardy–Weinberg equilibrium (HWE) was assessed by the $x^2$goodness-of-fit test. odds ratios (OR) with 95% confidence interval (CI) was used to assess the associations of *CETP* polymorphism with CAD risk. Logistic regression was used to determine the difference in lipid profiles among genotypes, adjusting for age, gender, smoking, EH, and DM. The statistic analyses were performed using the statistic software package SPSS 17.0 (SPSS Inc., Chicago, IL). A *P* value less than .05 (2-tailed) was regarded as statistically significant.

## 3. Results

### 3.1. The clinical characteristics between CAD group and controls

The baseline characteristics of patients with CAD and control subjects are presented in Table 1. CAD patients were significantly older and had higher frequencies of male, EH, DM, and current smoker than controls. In comparison with the control subjects, CAD patients had significantly higher TC, LDL-C, ApoB, non-HDL-C, AI, and AIP. In contrast, HDL-C and ApoA1 levels were decreased in CAD patients compared to controls. No significant differences were found in TG levels between CAD and control subjects.

**Table 1**

**Clinical characteristics of 2 studied populations.**

| Characteristics | CAD (n = 556) | Controls (n = 414) | P |
|---|---|---|---|
| Age, years | 64.24 ± 9.94 | 61.49 ± 9.11 | <.001 |
| Male [n(%)] | 391 (70.32) | 214 (50.69) | <.001 |
| EH [n(%)] | 404 (70.66) | 242 (58.45) | <.001 |
| DM [n(%)] | 142 (25.54) | 61 (14.73) | <.001 |
| Current smoker [n(%)] | 213 (38.31) | 104 (25.12) | <.001 |
| TC, mmol/L | 4.59 ± 1.05 | 4.44 ± 0.95 | .026 |
| TG, mmol/L | 1.45 (1.05–2.10) | 1.39 (0.97–2.09) | .104 |
| HDL-C, mmol/L | 1.08 ± 0.27 | 1.17 ± 0.31 | <.001 |
| LDL-C, mmol/L | 2.94 ± 0.93 | 2.66 ± 0.80 | <.001 |
| ApoAI, g/L | 1.17 ± 0.22 | 1.24 ± 0.24 | <.001 |
| ApoB, g/L | 0.97 ± 0.29 | 0.91 ± 0.26 | .001 |
| non-HDL-C, mmol/L | 3.51 ± 0.15 | 3.28 ± 0.91 | <.001 |
| AI | 3.48 ± 1.46 | 3.00 ± 1.14 | <.001 |
| AIP | 0.16 ± 0.31 | 0.11 ± 0.32 | .012 |

Data are expressed as mean ± standard deviation (SD) or number (Percentage); AI = atherosclerosis index, AIP = atherogenic index of plasma, Apo = apolipoprotein, CAD = coronary artery disease, DM = diabetes mellitus, EH = essential hypertension, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride.

### 3.2. Distribution of the genotypic and allelic frequencies in CAD and control groups

The genotypic distributions in cases and controls did not deviate from the Hardy-Weinberg equilibrium ($P > .05$). As shown in Table 2, the genotype and allele distributions of the *CETP* rs708272 were not significantly different between the patients with CAD and control subjects ($P > .05$). No association was found between *CETP* rs708272 polymorphism and CAD risk in different comparative models (Table 3). The frequency of T allele was 41.91% in CAD patients and 41.79% in controls. When the subgroup analyses according to gender and ages (<60 years and ≥60 years) were carried out, still no significant associations between *CETP* rs708272 and the risk of CAD were observed (Supplement Table 2, http://links.lww.com/MD/C676).

### 3.3. Effects of CETP rs708272 polymorphism on lipid levels and comprehensive lipid index

As shown in Table 4, participants with TT genotype had higher HDL-C levels (1.17 ± 0.31 mmol/L vs 1.09 ± 0.29 mmol/L, $P = .001$) and lower AIP levels (0.08 ± 0.35 vs 0.16 ± 0.31, $P = .004$) compared with those with CC genotype in the whole population, after adjusting for age, gender, smoking, EH, and DM. The T allele carriers had higher HDL-C levels than the T allele non-carriers (1.13 ± 0.29 mmol/L vs 1.09 ± 0.29 mmol/L, $P = .023$). Furthermore, subgroup analyses based on gender were carried out. In males, the results showed that participants with TT genotype had significantly higher HDL-C levels and lower AIP levels compared with CC genotype ($P < .05$). In addition, males with CT+TT genotypes had higher HDL-C levels and lower AIP levels than those with CC genotypes (HDL-C: CT+TT 1.11 ± 0.31 vs CC 1.06 ± 0.30 mmol/L, $P = .041$; AIP: CT+TT 0.12 ± 0.32 vs CC 0.16 ± 0.31, $P = .034$, respectively). However, there were no significant associations between *CETP* rs708272 polymorphism and lipid profiles in females, after adjusting for confounders.

**Table 2**

**Distribution of *CETP* rs708272 polymorphism in CAD patients and control subjects.**

| | CAD (n = 556) | Controls (n = 414) | $\chi^2$ | P |
|---|---|---|---|---|
| Genotypes | | | | |
| CC | 195 | 148 | 0.120 | .942 |
| CT | 256 | 186 | | |
| TT | 105 | 80 | | |
| Alleles | | | | |
| C | 646 | 482 | 0.003 | .963 |
| T | 466 | 346 | | |
| Dominant model | | | | |
| CC+CT | 451 | 334 | 0.030 | .869 |
| TT | 105 | 80 | | |
| Recessive model | | | | |
| CC | 195 | 148 | 0.048 | .839 |
| CT+TT | 361 | 266 | | |

**Table 3**

**Association between *CETP* rs708272 polymorphism in CAD patients and control subjects.**

| | CAD (n = 556) | Controls (n = 414) | OR (95% CI)* | P* |
|---|---|---|---|---|
| Genotypes | | | | |
| CC | 195 | 148 | 1 | |
| CT | 256 | 186 | 0.978 (0.724–1.320) | .884 |
| TT | 105 | 80 | 0.963 (0.658–1.409) | .847 |
| Dominant model | | | | |
| CC+CT | 451 | 334 | 1 | |
| TT | 105 | 80 | 0.975 (0.693–1.373) | .886 |
| Recessive model | | | | |
| CC | 195 | 148 | 1 | |
| CT+TT | 361 | 266 | 0.974 (0.736–1.288) | .851 |

CAD = coronary artery disease, CI = confidence interval, OR = odds ratios.
* adjustment for age, gender, smoking, EH and DM.

## 4. Discussion

To our knowledge, this is the first study to explore the effect of *CETP* rs708272 polymorphism on comprehensive lipid index in Chinese population. Our present study revealed that carriers with the minor T allele had lower AIP levels than those with CC genotype in males.

CETP alters the lipid levels by mediating the inverse transfer of cholesterol and affects the susceptibility to CAD, which has been widely investigated in vivo. The expression and activity of CETP were influenced by *CETP* gene polymorphisms. In recent years, a lot of clinical studies had explored the relationship between rs708272 polymorphism and the risk of cardiovascular disease and lipid levels.[25,26] But the results were inconsistent in different countries. Even in the same country, the results were also controversial.[20] In 2017, Abdel Maksoud et al found that *CETP* rs708272 polymorphism decreased the risk of unstable angina in Egyptian national patients.[26] Vargas-Alarcon et al revealed that this variant was not only associated with the risk of acute coronary syndrome but also with HDL-C levels and HDL subclasses in Mexican mestizos.[27] However, a prospective population-based study conducted in Caucasians demonstrated that *CETP* rs708272 was associated with increased levels of HDL-C, but not a decreased risk for CAD.[28] To avoid the poorly statistic efficiency caused by small sample size, several meta-analysis studies were also performed to clarity the associations of *CETP* rs708272 polymorphism and CAD risk and lipid levels. But, they also concluded the contradictory results.[19,21] In 2016, Guo et al performed a meta-analysis to

**Table 4**

**Effect of *CETP* rs708272 polymorphism on lipid levels and comprehensive lipid indexes.**

| | TC, mmol/L | TG, mmol/L | HDL-C, mmol/L | LDL-C, mmol/L | ApoAI, g/L | ApoB, g/L | AI | AIP |
|---|---|---|---|---|---|---|---|---|
| Whole (n=970) | | | | | | | | |
| CC (n=343) | 4.49±1.04 | 1.46 (1.01–2.16) | 1.09±0.29 | 2.77±0.88 | 1.20±0.24 | 0.94±0.28 | 3.36±1.53 | 0.16±0.31 |
| CT (n=442) | 4.52±0.97 | 1.47 (1.02–2.03) | 1.11±0.28 | 2.84±0.86 | 1.19±0.22 | 0.94±0.28 | 3.26±1.25 | 0.14±0.31 |
| TT (n=185) | 4.62±1.06 | 1.29 (0.97–2.09) | 1.17±0.31 | 2.87±0.96 | 1.20±0.23 | 0.95±0.30 | 3.15±1.23 | 0.08±0.35 |
| *P1*[*] | 0.522 | 0.854 | 0.193 | 0.220 | 0.733 | 0.803 | 0.389 | 0.551 |
| *P2*[*] | 0.119 | 0.265 | 0.001 | 0.184 | 0.183 | 0.817 | 0.079 | 0.004 |
| CT+ TT (n=627) | 4.55±1.00 | 1.41 (1.00–2.06) | 1.13±0.29 | 2.85±0.89 | 1.20±0.22 | 0.95±0.28 | 3.22±1.24 | 0.12±0.32 |
| *P3*[*] | 0.265 | 0.550 | 0.023 | 0.447 | 0.776 | 0.772 | 0.169 | 0.107 |
| Male (n=605) | | | | | | | | |
| CC (n=206) | 4.40±1.00 | 1.45 (1.03–2.22) | 1.06±0.30 | 2.72±0.86 | 1.17±0.24 | 0.94±0.28 | 3.36±1.53 | 0.16±0.31 |
| CT (n=281) | 4.36±0.95 | 1.35 (0.98–1.85) | 1.09±0.29 | 2.77±0.85 | 1.15±0.22 | 0.91±0.27 | 3.22±1.29 | 0.13±0.32 |
| TT (n=118) | 4.64±1.17 | 1.27 (0.92–2.16) | 1.18±0.33 | 2.90±1.10 | 1.22±0.22 | 0.96±0.32 | 3.18±1.30 | 0.08±0.38 |
| *P1*[*] | 0.856 | 0.407 | 0.346 | 0.515 | 0.444 | 0.526 | 0.261 | 0.194 |
| *P2*[*] | 0.053 | 0.106 | 0.001 | 0.113 | 0.060 | 0.527 | 0.125 | 0.004 |
| CT+ TT (n=399) | 4.44±1.02 | 1.32 (0.97–1.93) | 1.11±0.31 | 2.81±0.93 | 1.17±0.22 | 0.93±0.29 | 3.22±1.24 | 0.12±0.32 |
| *P3*[*] | 0.498 | 0.328 | 0.041 | 0.259 | 0.835 | 0.849 | 0.136 | 0.034 |
| Female (n=365) | | | | | | | | |
| CC (n=137) | 4.62±1.09 | 1.49 (1.00–2.11) | 1.13±0.28 | 2.84±0.91 | 1.25±0.25 | 0.95±0.27 | 3.41±1.64 | 0.18±0.31 |
| CT (n=161) | 4.79±0.95 | 1.56 (1.17–2.32) | 1.15±0.26 | 2.98±0.86 | 1.26±0.20 | 1.00±0.27 | 3.33±1.17 | 0.17±0.28 |
| TT (n=67) | 4.57±0.85 | 1.35 (1.03–1.91) | 1.16±0.28 | 2.82±0.67 | 1.23±0.24 | 0.92±0.24 | 3.09±1.08 | 0.08±0.27 |
| *P1*[*] | 0.182 | 0.340 | 0.376 | 0.200 | 0.768 | 0.227 | 0.869 | 0.425 |
| *P2*[*] | 0.803 | 0.286 | 0.443 | 0.962 | 0.647 | 0.374 | 0.309 | 0.236 |
| CT+ TT (n=228) | 4.73±0.92 | 1.53 (1.12–2.14) | 1.16±0.26 | 2.93±0.81 | 1.25±0.21 | 0.97±0.27 | 3.21±1.29 | 0.11±0.34 |
| *P3*[*] | 0.350 | 0.721 | 0.330 | 0.333 | 0.965 | 0.545 | 0.785 | 0.895 |

AI = atherosclerosis index, AIP = atherogenic index of plasma, Apo = apolipoprotein, HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol, *P*1 = CT verses CC, *P*2 = TT verses CC, *P*3 = CT+TT verses CC, TC = total cholesterol, TG = triglyceride.

[*] adjustment for age, gender, smoking, EH, and DM.

explore the associations of the *CETP* TaqIB polymorphism with the levels of HDL-C and the composite ischemic CVD risk.[19] They found that carriers of B2B2 genotype had a lower risk of composite ischemic CVD than non-carriers and higher concentrations of HDL-C than carriers of the B1B1 genotype in both Asians and Caucasians. On the contrary, in a meta-analysis of 15,055 subjects, no association between the *CETP* rs708272 polymorphism and CAD was observed under any comparative models in the whole Chinese population.[20] Subgroup analysis stratified by the ethnicity showed that a significant association between them was observed in Chinese Han subgroup, whereas in non-Han subgroup. In the present study, we did not find an association of *CETP* rs708272 polymorphism and the CAD risk in any genetic comparison models. Subgroup analyses based on age and gender also suggested that no significant association between them existed. However, there was significant difference in HDL-C levels among 3 genotypes in the whole population and the T allele carriers had higher HDL-C levels than non-carriers. Our result was consistent with previous studies.

There was gender difference in the association between *CETP* rs708272 polymorphism and serum lipid levels.[29,30] In 2000, Kark et al revealed that the Taq1 B allele was significantly inverse associated with HDL-C and Apo A1 in women, rather than in man.[31] In another study, the minor B2B2 genotype was found associated with elevated HDL-C in obese women.[32] The gender specific association may reflect dissimilarities in the regulatory function of CETP in lipid exchange. In our subgroup analyses based on gender revealed that the significant difference in HDL-C ApoA1 levels among genotypes only existed in males. Males with T allele had higher HDL-C levels than those with CC genotypes, which suggested a gender-specific effect of *CETP* rs708272 polymorphism on lipid levels in Chinese population. Our results were inconsistent with Kark et al's study, which might be due to different ethnicity or complicated geno-environmental interactions. In addition, mean age in our study was older than that in Kark et al's study, which might also lead to the discrepancy. Moreover, because number of female was relatively small in our study, we should interpret the results cautiously.

As a novel comprehensive lipid index, AIP was calculated as logarithmic transformation of the ratio of TG to HDL-C.[23] Researches had shown that AIP was a novel and better biomarker associated with obesity and positively associated with the risk of all-cause death in elderly women.[8,33] It might be a better predicting factor to CAD than traditional lipid levels. In 2017, Noumegni et al found that AIP was significantly associated with the risk of cardiovascular disease in Cameroonian HIV-infected people after adjusting for socio-demographic, clinical and other biological factors.[34] AIP level was positively and strongly associated with obesity in a Chinese population and controlling the AIP level might be helpful for the prevention of obesity.[8] In our previous study, we also found that AIP was a strong and independent predictor for CAD in Chinese population.[9] Until now, no study was conducted to elucidate the relationship between rs708272 and comprehensive lipid index. In the present study, we found that carriers with T allele had lower AIP than non-carriers. Subgroup analysis based on gender revealed that only males with T allele had lower AIP, which suggested the gender-specific effect of *CETP* rs708272 polymorphism on AIP level.

Several limitations in our study need to be addressed. First of all, the sample size in our study was not big enough. Second, all of the subjects enrolled from hospital and underwent CAG examination, did not represent the general population. Third, CAD susceptibility and lipid levels were both influenced by

genetic and environmental factors, which were not comprehensively explored in our study.

## 5. Conclusions

Our results suggest that *CETP* rs708272 polymorphism has a gender-specific effect on lipid and AIP levels but not on the risk of CAD. Future studies with larger sample sizes and multi-centers are needed to confirm our findings.

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## Author contributions

**Conceptualization:** Gaojun Cai, Ganwei Shi.
**Data curation:** Gaojun Cai, Zhiying Huang.
**Formal analysis:** Gaojun Cai.
**Funding acquisition:** Gaojun Cai.
**Investigation:** Zhiying Huang.
**Methodology:** Ganwei Shi.
**Project administration:** Gaojun Cai.
**Resources:** Gaojun Cai.
**Software:** Gaojun Cai.
**Supervision:** Gaojun Cai.
**Validation:** Gaojun Cai.
**Visualization:** Gaojun Cai.
**Writing – original draft:** Gaojun Cai, Ganwei Shi.

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