Contribution of CYP24A1 variants in coronary heart disease among the Chinese population

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Abstract

Background: Cytochrome P450 (CYPs) participate in the mechanisms of cardiovascular disease. The purpose of this research was to evaluate the contributions of CYP24A1 variants to coronary heart disease (CHD) among the Chinese Han population.

Methods: This study included 505 CHD cases and 508 controls. Four variants of CYP24A1 (rs2762934, rs1570669, rs6068816 and rs2296241) were chosen and genotyped by the Agena MassARRAY system among the Chinese population. The linkage between CYP24A1 variants and CHD risk were assessed by logistic regression to compute the odds ratio (OR) and 95% confidence interval (CI). Then, multifactor dimensionality reduction (MDR) was applied to analyze the interactions of CYP24A1 variants.

Results: The results of this study showed that CYP24A1 rs6068816 significantly enhanced CHD risk in multiple genetic models (allele: \( P = 0.014 \); codominant: \( P = 0.015 \); dominant: \( P = 0.043 \); recessive: \( P = 0.040 \); additive: \( P = 0.013 \)), whereas rs2296241 was likely to protect individuals from CHD (codominant: \( P = 0.019 \); recessive: \( P = 0.013 \); additive: \( P = 0.033 \)). Stratification analysis revealed that CYP24A1 polymorphisms had strong relationships with CHD risk that were dependent on age, sex, Gensini grade and smoking status (\( P < 0.05 \)). Moreover, a four-locus model (rs2762934, rs1570669, rs6068816 and rs2296241) had significant impact on CHD risk in MDR analysis.

Conclusion: It revealed that CYP24A1 variants were significantly linked with CHD susceptibility in the Chinese population.

Keywords: Coronary heart disease, CYP24A1, Genetic polymorphisms, Case-control study, Stratified analysis, Multifactor dimensionality reduction, Chinese Han population

Introduction

Coronary heart disease (CHD) is a complex chronic inflammatory disease that is characterized by coronary artery remodeling and stenosis [1]. CHD is the leading cause of mortality and disability worldwide [2]. The World Health Organization reported that approximately 700,000 individuals die of CHD in China each year [3]. Previous studies have suggested that age, sex, diabetes and lifestyle factors (lack of exercise, smoking or alcohol use) are associated with susceptibility to CHD. CHD is a complex and heterogeneous illness that is attributed to the interaction of environmental and genetic factors, where the genetic factors are estimated to account for 30–60% of CHD risk [4, 5]. However, the role of genetic/environmental interactions in the development and progression of CHD requires further clarification.

Cytochrome P450 24 subfamily A member 1 (CYP24A1) encodes a 24-hydroxylase for degrading the active form of vitamin D through multiple pathways [6, 7].
The CYP450 proteins are monoxygenases that can catalyze reactions related to drug metabolism and lipid synthesis. It has been reported that the loss of CYP24A1 function resulted in increased serum concentration of 1, 25-dihydroxyvitamin D [7]. Previous studies revealed that vitamin D deficiency is a serious factor in the progression of cardiovascular disease [8–11]. In addition, CYP24A1 polymorphisms were associated with many diseases, such as stroke, hypertension, hepatitis C virus infection and cancers. Wei Yang et al. reported that rs1570669 was linked to a reduced risk of CYP24A1 in multiple diseases, this study assumed that CYP24A1 polymorphisms might be related to CHD risk. This study conducted a genetic association analysis of CYP24A1 polymorphisms (rs2762 934, rs1570669, rs6068816 and rs2296241) with CHD risk in the Chinese population.

Considering the role of CYP24A1 in multiple diseases, this study assumed that CYP24A1 polymorphisms might be related to CHD risk. This study conducted a genetic association analysis of CYP24A1 polymorphisms (rs2762 934, rs1570669, rs6068816 and rs2296241) with CHD risk in the Chinese population.

Methods

Study subjects

This study included 505 patients with CHD and 508 age- and sex-matched controls. CHD patients were recruited from Yanan University Affiliated Hospital in China. CHD patients were diagnosed as having angiographically demonstrated stenosis (≥ 50%) in one or more major coronary arteries by two experienced interventional cardiologists. The healthy controls were also collected from the Healthy Center of Yanan University Affiliated Hospital. All controls were determined to be free of cardiovascular disease. Individuals with inflammatory diseases, cardiomyopathy, renal diseases (detected by hematuria tests) or other severe diseases were excluded from this study. Characteristics of the study subjects were collected by medical records and questionnaires, including age, sex, smoking and alcohol use, duration of CHD, complications, and levels of low-density lipoprotein (LDL), high-density lipoprotein (HDL), uric acid (UA), urea, platelet (PLT), white blood cells (WBC), red blood cells (RBC), hemoglobin (HGB), triglyceride (TG) and total cholesterol (TC). The study was performed in agreement with the Ethics Committee of Yanan University Affiliated Hospital, and written informed consent was obtained from study subjects.

Single nucleotide polymorphisms (SNP) genotyping

According to the criteria of minor allele frequency (MAF) ≥ 0.05, four variants of CYP24A1 (rs2762934, rs1570669, rs6068816 and rs2296241) were selected according to the HapMap database (http://www.hapmap.org). Then, blood samples were collected, and genomic DNA was extracted by a blood DNA kit (GoldMag Co. Ltd., Xi’an, China). Four variants were genotyped with the Agena MassARRAY system (Agena, San Diego, CA, USA). The primers of CYP24A1 variants were designed by the Agena MassARRAY Assay Design 3.0 (San Diego, CA, USA; Supplementary Table 1). Agena Typer 4.0 Software (San Diego, CA, USA) was used for data management and analysis.

Data analysis

SPSS 21.0 software (SPSS, Chicago, IL, USA) was applied to compute data, and the significance threshold was set at P < 0.05. The variables were compared by Student’s t-test and chi-square analysis, individually. Fisher’s exact test was used to evaluate the Hardy-Weinberg equilibrium (HWE) of each SNP in healthy controls. The relationship of CYP24A1 polymorphisms and CHD susceptibility was assessed by logistic regression after adjustment for age and sex. This study determined the differences by an odds ratio (OR) with a 95% confidence interval (CI). Haplotype analysis of CYP24A1 polymorphisms and CHD risk was further analyzed using Haploview and PLINK software. Multifactor dimensionality reduction (MDR, version 3.0.1) was conducted to assess the impact of CYP24A1 polymorphisms on CHD susceptibility [14–16].

Results

Characteristics of the study population

Characteristics of the study individuals are shown in Table 1. This study enrolled 505 cases and 508 controls from China. The average ages of the two groups were 62.2 ± 10.4 and 61.5 ± 8.9 years old, respectively. The distributions of age and sex were similar between the case and control groups (age: p = 0.609; sex: P = 1.000). The levels of WBC, RBC, HGB, TG and TC in the two groups had significant differences (P < 0.05). Supplementary Table 2 did not show significant relationships between genotypes of CYP24A1 variants and clinical characteristics of CHD cases (P > 0.05).

Association of CYP24A1 polymorphisms and CHD risk

Four SNPs were genotyped in two groups, and all SNPs in the control group were HWE compliant (HWE P > 0.05, Table 2). For CYP24A1 rs6068816, the frequency distribution of the T allele was higher in CHD patients than that in healthy controls (P = 0.014). HaploReg showed that CYP24A1 polymorphisms were regulated by Enhancer histone marks, DNAs, motifs, proteins bound, motifs changed, NHGRI/EBI GWAS hits, SiPhy cons and Selected eQTL hits. Table 3 revealed that rs6068816 significantly increased CHD susceptibility in codominant
Table 1 Characteristics of the study population

| Variables | Cases (n = 505) | Controls (n = 508) | P |
|-----------|----------------|-------------------|---|
| Age, years |               |                   |   |
| > 60      | 280 (55%)     | 286 (56%)         |   |
| ≤ 60      | 225 (45%)     | 222 (44%)         |   |
| Sex       |               |                   |   |
| Male      | 334 (66%)     | 335 (66%)         | 1.00 |
| Female    | 171 (34%)     | 173 (34%)         |   |
| Smoking   |               |                   |   |
| Yes       | 230 (46%)     | 112 (22%)         |   |
| No        | 185 (37%)     | 153 (30%)         |   |
| Drinking  |               |                   |   |
| Yes       | 52 (10%)      | 109 (21%)         |   |
| No        | 303 (60%)     | 98 (19%)          |   |
| Hypertension |          |                   |   |
| Yes       | 315 (62%)     |                   |   |
| No        | 190 (38%)     |                   |   |
| Duration, months | |                   |   |
| ≥ 40      | 99 (20%)      |                   |   |
| < 40      | 232 (46%)     |                   |   |
| LDL (mmol/L) |            |                   |   |
| 2.59 ± 0.84 | 2.60 ± 0.73 | 0.932              | |
| HDL (mmol/L) |            |                   |   |
| 1.10 ± 0.27 | 1.14 ± 0.23 | 0.115              | |
| PLT (10^9/L) |          |                   |   |
| 197.73 ± 59.62 | 207.30 ± 53.92 | 0.059              | |
| WBC       | 6.89 ± 2.17   | 5.71 ± 1.41       | < 0.001 |
| RBC       | 4.32 ± 0.61   | 4.73 ± 0.47       | < 0.001 |
| HGB       | 134.31 ± 19.54 | 144.26 ± 17.74 | < 0.001 |
| Urea      | 5.22 ± 2.25   | 7.50 ± 24.60      | 0.096 |
| UA (μmol/L) |          |                   |   |
| 307.22 ± 92.67 | 318.73 ± 84.87 | 0.146              | |
| TG (mmol/L) |            |                   |   |
| 1.55 ± 0.90 | 1.81 ± 1.65 | 0.022              | |
| TC (mmol/L) |            |                   |   |
| 4.03 ± 0.96 | 5.39 ± 0.98 | 0.001              | |

HDL high-density lipoprotein, LDL low-density lipoprotein, PLT platelet, WBC white blood cells, RBC red blood cells, HGB hemoglobin, UA uric acid, TG triglyceride, TC total cholesterol

Variables are presented as the mean ± SD

Bold-faced values indicate significant difference (P < 0.05)

Table 2 Allele frequency of CYP24A1 SNPs and their associations with risk of CHD

| SNP      | Genotype | Location | Cases | Controls | MAF-Case | MAF-Control | HWE P | OR(95%CI) P | HaploReg |
|----------|----------|----------|-------|----------|----------|-------------|-------|-------------|---------|
| rs2762934 | A/G      | 3’-UTR   | 116/800 | 108/908 | 0.115    | 0.106       | 1.000 | 1.00 (0.83–1.15) | 0.519 Enhancer histone marks, DNAse, Motifs, Proteins bound, Motifs changed |
| rs1570669 | A/G      | Intron   | 379/629 | 401/615 | 0.376    | 0.395       | 0.403 | 0.92 (0.77–1.11) | 0.388 DNAse, Proteins bound, Motifs changed, \texttt{NHGRI/EBI GWAS hits} |
| rs6068816 | T/C      | Synonymous| 380/622 | 330/680 | 0.379    | 0.327       | 0.920 | 1.26 (1.05–1.51) | 0.014 \texttt{SiPhy cons, DNAse, Proteins bound, Motifs changed} |
| rs2296241 | A/G      | Synonymous| 423/587 | 469/547 | 0.419    | 0.462       | 0.212 | 0.84 (0.71–1.00) | 0.052 \texttt{SiPhy cons, Enhancer histone marks, DNAse, Proteins bound, Motifs changed, Selected eQTL hits} |

SNP single nucleotide polymorphism, CHD coronary heart disease, MAF minor allele frequency, OR odds ratio, 95% CI 95% confidence interval

Bold-faced values indicate significant difference (P < 0.05)

Discussion

This study investigated the relationship of four CYP24A1 SNPs (rs2762934, rs1570669, rs6068816 and rs2296241) with CHD risk.
Table 3 Genotypes frequencies of CYP24A1 SNPs and their associations with risk of CHD

| SNP       | Genotype | Cases | Controls | Without adjustment | With adjustment |
|-----------|----------|-------|----------|--------------------|-----------------|
|           |          | OR(95%CI) | P* | OR(95%CI) | Pb |
| rs2762934 |          |        |          |        |     |
| co-dominant | AA      | 4     | 5        | 0.83 (0.22–3.11) | 0.781           | 0.80 (0.21–3.02) | 0.745 |
|           | GA      | 108   | 98       | 1.14 (0.84–1.55) | 0.398           | 1.13 (0.83–1.54) | 0.436 |
|           | GG      | 391   | 405      | 1        | 1    | 1    | 1    |
| dominant  | AA-AG   | 112   | 103      | 1.13 (0.83–1.52) | 0.439           | 1.11 (0.82–1.51) | 0.484 |
|           | GG      | 391   | 405      | 1        | 1    | 1    | 1    |
| recessive | AA      | 4     | 5        | 0.81 (0.22–3.02) | 0.750           | 0.78 (0.21–2.94) | 0.716 |
|           | AG-GG   | 499   | 503      | 1        | 1    | 1    | 1    |
| additive  |         | 1.1   | (0.83–1.46) | 0.512 | 1.09 (0.82–1.44) | 0.563 |
| rs1570669 |          |        |          |        |     |
| co-dominant | AA      | 75    | 74       | 0.92 (0.63–1.34) | 0.655           | 0.91 (0.62–1.33) | 0.637 |
|           | GA      | 229   | 253      | 0.82 (0.63–1.07) | 0.146           | 0.82 (0.63–1.07) | 0.150 |
|           | GG      | 200   | 181      | 1        | 1    | 1    | 1    |
| dominant  | AA-AG   | 304   | 327      | 0.84 (0.65–1.09) | 0.184           | 0.84 (0.65–1.09) | 0.184 |
|           | GG      | 200   | 181      | 1        | 1    | 1    | 1    |
| recessive | AA      | 75    | 74       | 1.03 (0.72–1.45) | 0.888           | 1.02 (0.72–1.44) | 0.914 |
|           | AG-GG   | 429   | 434      | 1        | 1    | 1    | 1    |
| additive  |         | 0.92  | (0.77–1.11) | 0.386 | 0.92 (0.77–1.10) | 0.378 |
| rs6068816 |          |        |          |        |     |
| co-dominant | TT      | 74    | 53       | 1.63 (1.09–2.44) | 0.017           | 1.64 (1.10–2.46) | 0.015 |
|           | TC      | 232   | 224      | 1.21 (0.93–1.58) | 0.157           | 1.21 (0.93–1.58) | 0.152 |
|           | CC      | 195   | 228      | 1        | 1    | 1    | 1    |
| dominant  | TT-TC   | 306   | 277      | 1.29 (1.01–1.66) | 0.046           | 1.30 (1.01–1.67) | 0.043 |
|           | CC      | 195   | 228      | 1        | 1    | 1    | 1    |
| recessive | TT      | 74    | 53       | 1.48 (1.01–2.15) | 0.042           | 1.49 (1.02–2.17) | 0.040 |
|           | TC-CC   | 427   | 452      | 1        | 1    | 1    | 1    |
| additive  |         | 1.26  | (1.05–1.51) | 0.014 | 1.26 (1.05–1.52) | 0.013 |
| rs2296241 |          |        |          |        |     |
| co-dominant | AA      | 71    | 101      | 0.64 (0.44–0.94) | 0.023           | 0.63 (0.43–0.93) | 0.019 |
|           | GA      | 281   | 267      | 0.96 (0.73–1.28) | 0.795           | 0.95 (0.71–1.26) | 0.702 |
|           | GG      | 153   | 140      | 1        | 1    | 1    | 1    |
| dominant  | AA-AG   | 352   | 368      | 0.88 (0.67–1.15) | 0.337           | 0.86 (0.65–1.13) | 0.280 |
|           | GG      | 153   | 140      | 1        | 1    | 1    | 1    |
| recessive | AA      | 71    | 101      | 0.66 (0.47–0.92) | 0.014           | 0.66 (0.47–0.92) | 0.013 |
|           | AG-GG   | 434   | 407      | 1        | 1    | 1    | 1    |
| additive  |         | 0.82  | (0.68–0.99) | 0.041 | 0.82 (0.68–0.98) | 0.033 |

SNP single nucleotide polymorphism, CHD coronary heart disease, OR odds ratio, 95% CI 95% confidence interval
P* values were calculated by logistic regression analysis with the comparison between CHD patients and healthy controls
Pb values were calculated by logistic regression analysis with adjustment for age and gender
Bold-faced values indicate significant difference (P < 0.05)

on CHD risk; rs6068816 and rs2296241 indicated susceptibility to CHD in the Chinese Han population (P < 0.05). Subgroup analysis demonstrated that rs2762934 enhanced CHD risk among younger individuals (age ≤ 60), rs2296241 decreased the risk of CHD among men, and rs6068816 was significantly linked with a higher risk of CHD in the subgroups of age ≤ 60, men, and smokers. For CHD patients, rs1570669 could enhance CHD risk in the subgroup of Gensini grade. It also showed one block (rs2762934 and rs1570669). These results might provide a
new insight on the contribution of CYP24A1 polymorphisms in CHD risk among the Chinese population.

Vitamin D is a soluble steroid hormone that plays an important role in calcium homeostasis, skeletal health and cardiovascular pathophysiology [2]. It has been reported that low levels of vitamin D are linked with a variety of diseases, including diabetes, autoimmune disorders, skin diseases, cardiovascular diseases and cancers [17–19]. Vitamin D is produced in the skin and is metabolized in the liver and kidney, which requires CYP450 enzymes, such as CYP2R1, CYP27B1, CYP24A1 [20]. Previous studies indicated that rs6068816 affected cancer risk through the vitamin D pathway [21, 22] and that rs2296241 was related to vitamin D deficiency in the development of food sensitization [23]. The study mainly focused on the linkage of CYP24A1 and CHD among the Chinese Han population. The results showed CYP24A1 polymorphisms were associated with CHD susceptibility. CYP24A1 rs6068816 significantly increased the risk of CHD, whereas no significant linkage of hypertension with rs6068816 and no difference in vitamin D levels among the genotypes of rs6068816 were found [24]. Moreover, this study suggested that rs2296241 could protect individuals from CHD. Lu et al. also reported that rs2296241 had strong associations with systolic blood pressure (BP), diastolic BP, pulse pressure, or mean arterial pressure in the Women’s Genome Healthy Study [25]. These findings suggest that CYP24A1 polymorphisms may participate in the progression of CHD, and this is likely due to the effects of CYP24A1 on regulating the levels of vitamin D. Further studies are required to verify these results.

There are differences between the influence of age and sex on CHD; CHD more frequently occurs in men (17.6%) than women (10.6%) [26]. The mortality of CHD is also different in adults between the two sexes, and it increases with age [27]. However, the causes of age and sex differences in CHD are still unclear. Hence, this study evaluated the influences of CYP24A1 polymorphisms on CHD risk in the subgroups of age and sex. The impact of rs2762934, rs6068816 and rs2296241 on

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Table 4 Stratification analyses of the association of CYP24A1 polymorphisms with susceptibility of CHD

| Polymorphisms | Subgroups | Homozygote | Heterozygote | Dominant | Recessive | Additive | Allele |
|--------------|-----------|------------|--------------|----------|-----------|----------|--------|
|              | OR (95%CI) | P          | OR (95%CI)   | P        | OR (95%CI) | P        | OR (95%CI) | P     |
| rs2762934    | Age (≤ 60) |            |              |          |           |          |        |        |
|              | –         | 1.51       | 0.090        | 1.57     | 0.060     | 1.61     | 0.040  | 1.57   | 0.048 |
|              | (0.93–2.44)| (0.97–2.53)| (0.82–2.14)  | (0.24–0.85) | (1.01–2.56) | (1.00–2.46) |         |
| rs1570669    | Genotype  | 0.61       | 1.79         | 1.33     | 1.45      | 0.92     | 0.637  | 0.90   | 0.544 |
|              | (0.31–1.20)| (1.06–3.02)| (0.82–2.14)  | (0.24–0.85) | (0.66–1.29) | (0.64–1.26) |         |
| rs6068816    | Age (≤ 60) |            |              |          |           |          |        |        |
|              | –         | 1.27       | 0.250        | 1.49     | 0.040     | 2.42     | < 0.001| 1.53   | < 0.001|
|              | (0.85–1.90)| (1.01–2.18)| (1.01–2.18)  | (0.24–0.85) | (1.34–4.38) | (1.15–2.03) |         |
|              | Men       | 2.03       | 1.30         | 1.42     | 1.028     | 1.77     | 0.022  | 1.38   | 0.006 |
|              | (1.21–3.40)| (0.94–1.80)| (1.04–1.93)  | (1.09–2.88) | (1.10–1.74) | (1.09–1.72) |         |
|              | Smoker    | 0.007      | 0.116        | 0.92     | 0.060     | 0.85     | < 0.001| 1.57   | 0.011 |
|              | (0.04–0.90)| (0.82–2.16)| (0.98–2.49)  | (1.17–5.78) | (1.11–2.23) | (1.15–2.27) |         |
| rs2296241    | Men       | 0.031      | 0.77         | 0.73     | 0.059     | 0.71     | 0.099  | 0.77   | 0.027 |
|              | (0.37–0.96)| (0.54–1.09)| (0.52–1.01)  | (0.47–1.07) | (0.61–0.97) | (0.61–1.90) |         |

OR Odds ratio, CI Confidence interval, CHD coronary heart disease
Bold-faced values indicate significant difference (P < 0.05)
CHD risk varied with age and sex. In addition, smoking was a major risk factor for CHD [28]. The results showed that CYP24A1 rs6068816 significantly increased the risk of CHD among men, smokers and subjects aged 60 years old or younger. A meta-analysis involving 20,593 cases and 25,458 controls revealed that there were no associations of rs6068816 with overall cancer risks [13], but Wei Yang et al. reported that rs6068816 could enhance the susceptibility of ischemic stroke in the Chinese population [12]. These studies would provide insight on the diagnosis, prevention or treatment of cardiovascular disease. Last, the study divided CHD patients into different groups according to Gensini grade, and CYP24A1 rs1570669 could worsen the condition of patients. This finding gives us a clue as to individual treatments for CHD patients.

Study strength and limitations

The strengths of this study were listed as following. First, the study reported the linkage of CYP24A1 polymorphisms and CHD risk, and these impacts were related to multiple factors. Second, the association of genetic polymorphisms with CHD susceptibility was also assessed by many subgroups, as well as haplotype and MDR analysis. Third, this study used clinical data from a study population of 1013 individuals. Finally, the study provides a new candidate gene or variants for studying the subsequent pathogenesis of CHD. These findings may facilitate the diagnosis and prevention of CHD in the future.

There are some deficiencies in this study, which should be listed. First, sample size was relatively small, such that it could not give enough statistical power. Additionally, a selection bias may exist in this case-control study. Third, more risk indicators were not analyzed in the study due to limitations of information. Fourth, the study did not assay vitamin D levels in cases and controls. Finally, more studies should be performed to validate these results.

Conclusions

The study revealed that CYP24A1 variants were nominally linked with CHD susceptibility, and the impacts of CYP24A1 polymorphisms on CHD risk were related to age, sex, Gensini grade or smoking status. It suggested that CYP24A1 variants might take part in the development of CHD. It provides a scientific basis for the underlying mechanism of CHD. In the future, these findings will guide personalized medicine for the treatment of CHD.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12944-020-01356-x.

Additional file 1: Supplementary Table 1 Primers of CYP24A1 polymorphisms, Supplementary Table 2 Clinical characteristics of CHD patients based on CYP24A1 polymorphisms.

Table 5 MDR analysis of SNP-SNP interactions

| Model                          | Training Bal. Acc. | Testing Bal. Acc. | CV Consistency | Accuracy | Sensitivity | Specificity | OR(95%CI) | P      |
|-------------------------------|--------------------|-------------------|----------------|----------|-------------|------------|-----------|--------|
| rs2296241                     | 0.533              | 0.533             | 10/10          | 0.533    | 0.614       | 0.452      | 1.31 (1.02–1.68) | 0.035  |
| rs1570669;rs2296241            | 0.550              | 0.548             | 10/10          | 0.550    | 0.721       | 0.378      | 1.57 (1.20–2.05) | 0.001  |
| rs1570669;rs6068816;rs2296241  | 0.567              | 0.509             | 6/10           | 0.565    | 0.457       | 0.673      | 1.74 (1.35–2.24) | < 0.001|
| rs2762934;rs1570669;rs6068816;rs2296241 | 0.586 | 0.484 | 10/10 | 0.580 | 0.659 | 0.501 | 1.94 (1.51–2.50) | < 0.001|

MDR multifactor dimensionality reduction, SNP single nucleotide polymorphism, CV cross-validation, OR odds ratio, CI confidence interval

Bold-faced values indicate significant difference (P < 0.05)

Abbreviations

CHD: Coronary heart disease; CYP24A1: Cytochrome P450 24 subfamily A member 1; HDL: High-density lipoprotein; LDL: Low-density lipoprotein; UA: Uric acid; PLT: Platelet; WBC: White blood cells; RBC: Red blood cells; HGB: Hemoglobin; TG: Triglyceride; TC: Total cholesterol; MAF: Minor allele frequency; HWE: Hardy-Weinberg equilibrium; OR: Odds ratio; CI: 95% confidence interval; MDR: Multifactor dimensionality reduction; BP: Blood pressure

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Authors’ contributions

Gaorong Huang designed the experiment, Peng Qian and Xuanchao Cao performed the experiment, Xianjing Xu and Mingqin Duan processed the data, Peng Qian Wrote the manuscript, Qian Zhang revised the manuscript. The authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

This study protocol was approved by the Ethics Committee of the Yanan University Affiliated Hospital (CRD2017136845) and under the guidelines of
the Declaration of Helsinki. Written informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors have no conflicts of interest to report.

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