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Association of single nucleotide polymorphism rs2076185 in chromosome 6P24.1 with premature coronary artery diseases in Chinese Han population

Xin LIU, Min ZHANG, Hong-Wei SHAN, Xian-Tao SONG, Shu-Zheng LYU

Department of Cardiology, Beijing An Zhen Hospital, Capital Medical University and Beijing Institute of Heart Lung and Blood Vessel Disease, Beijing, China

Abstract

Objectives To study the association of single nucleotide polymorphism (SNP) rs2076185 in chromosome 6p24.1 with the premature coronary artery diseases (PCAD) in Chinese Han population. **Methods** A total of 1382 patients were divided into the PCAD group and the control group based on their coronary arteriography (CAG) results. Their SNP rs2076185 were analyzed by the mass-spectrometry. Their allele and genotype frequency in Hardy-Weinberg equilibrium were calculated for assessment. Logistic regression was employed to remove confounding factors and correlate SNP rs2076185 with PCAD. **Results** The allele and genotype frequencies of the control group were in Hardy-Weinberg equilibrium ($P > 0.05$). The frequencies of allele G of rs2076185 were 54.2% in the PCAD group and 49.5% in the control group. The difference was significant ($P = 0.042$). The genotype distribution of rs2076185 of the two groups was also significantly different. The univariate analysis showed that the rs2076185 polymorphisms were associated with the PCAD only in the additive model (OR: 0.828, 95% CI: 0.711–0.964, $P = 0.014$), and in the dominant model (OR: 0.753, 95% CI: 0.591–0.958, $P = 0.021$). After removing the confounding variables, the rs2076185 polymorphisms was associated with PCAD in the additive model (OR: 0.775, 95% CI: 0.648–0.928, $P = 0.005$), in the dominant model (OR: 0.698, 95% CI: 0.527–0.925, $P = 0.012$), and in the recessive model (OR: 0.804, 95% CI: 0.538–0.983, $P = 0.038$). **Conclusion** Allele G of rs2076185 reduces the PCAD risks in Chinese Han population, therefore it could be a coronary artery diseases protective factor in Chinese Han population.

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Keywords: Chinese Han population; Gene; Premature coronary artery disease; Single nucleotide polymorphism

1 Introduction

A new genetic analysis strategy, the Genome Wide Association Study (GWAS) has been developed since the preliminary completion of the Human Genome Project. It conducted the association analysis with multiple genes on popular genetic variations in order to identify any sequence variations, screening disease related single nucleotide polymorphisms (SNPs). Coronary artery disease (CAD) is an ischemic heart disease with morphological changes of coronary artery stenosis or occlusion caused by coronary artery atherosclerosis. It has been the leading cause of disability and death worldwide. It is estimated that the mortality rate of ischemic heart disease will account for 13.1% of the total deaths in 2030.[1] In China, the mortality of cardiovascular diseases in rural residents and urban residents have accounted for 41.1% and 41.5%, respectively, ranking top among all causes.[2] Prevention and treatment of CAD is urgent. However, CAD is different for populations of various nationalities due to its highly genetic heterogeneity. Thus, establishing GWAS for the Chinese Han population is valuable.

The research of GWAS of Chinese Han population has been on going in Asia. In 2011, the Human Genome Research Center of Huazhong University of Science & Technology published the first genome-wide association analysis on CAD of Chinese Han population in China after completing three phases of multi center GWAS by comparing 4583 cases of patients with coronary heart disease (CHD) and 3470 cases of the normal.[3] Two groups of samples from different geographic areas, Discovery population-Beijing and Discovery population-Hubei, were studied first by scanning their 447,094 SNPs with Affymetrix Genome-wide SNP 5.0 Array, then selecting 9 SNPs of consistent allele risks from the samples with a P value less than 0.01. Then, Taqman SNP point technology was employed to verify sample groups (572 CAD cases *vs.* 436 control). More groups of samples from more geographic areas (Replication population Shandong, 811 cases *vs.* 818 controls;

Correspondence to: Shu-Zheng LYU, MD, PhD, Department of Cardiology, Beijing An Zhen Hospital, Capital Medical University and Beijing Institute of Heart Lung and Blood Vessel Disease, Beijing 100029, China.
E-mail:shuzheng@medmail.com.cn

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Rep-Hubei, 1012 cases *vs.* 1732 controls; Rep-North, *vs.* 845cases 1367 controls) were finally studied, finding that 9p21.3 (rs1333048) and new 6p24.1 (rs6903956) are associated with CAD in the Chinese Han population. In 2012, researchers led by Xiang-Feng LU of the Population Genetics and Population Control Institute of Chinese Academy of Medical Sciences and Fuwai Cardiovascular Disease Hospital found four new susceptibility loci of CHD in the Chinese population.[4] Genome-wide association analysis was conducted on 509 CHD cases *vs*.1034 cases of the control using the high density Affymetrix 500K SNP microarray, and on 1034 CHD cases *vs.* 4245 cases of the control using Affymetrix CHB1 microarray. The Taqman quantitative PCR or SNP Sequenom genotyping technique were used on 15,460 patients with CHD and 11,472 individuals of the control to confirm that four SNP sites (rs2123536, rs1842896, rs9268402 and rs7136259) and their neighboring chromosomal regions (TTC32-WDR35, GUCY1a3, C6orf10-BTNL2 and ATP2B1) are susceptible to CAD incidence, as well as other susceptibility genes reported by others.[4]

Research on GWAS of CHD has been also conducted in other Asian countries. In 2013, A Singapore GWAS study on various ethnic groups (including Chinese, Malays and Indians) found SNP rs6903956 of the ADTRP gene located on chromosome 6p24.1 is associated with CHD.[5] In 2014, a research on the relationship between CDKN2A/B, ADTRP and PDGFD gene polymorphism and CHD in the Japanese population showed that ADTRP was an important risk factor for CHD but the risk alleles in the Japanese population and Chinese population are different.[6]

The genetic law shows that the genetic factor plays an important role in the development of CAD. The earlier the occurrence of a disease, the closer the genetic relationship is to the disease. According to ATPIII, CHD is premature when a CHD patient is younger (male < 55-year-old or female < 65-year-old).[7] Our study is focused on the comparison between the population of premature coronary artery disease (PCAD) and the population of the control who do not have any CHD. Our purpose is to find the gene polymorphism loci which are associated with CHD of Chinese Han population, unveiling more comprehensive features of the gene polymorphism in Chinese Han population and their roles in CHD genetics. This paper for the first time reports a statistic study to show SNP rs2076185 in chromosome 6p24.1 can be associated with PCAD in Chinese Han population.

2 Methods

2.1 Population

All the cases were from patients with CAG at the Department of Cardiology of Anzhen Hospital of Capital University of Medical Sciences from May 2011 to April 2014. The patients were divided into PCAD group of 636 patients and the control group of 746 healthy patients according to their CAG results. All the patients were confirmed to have been Chinese Han population for three generations. Males are younger than 45 years old and females are younger than 55 years old. To be part of the PCAD group, his or her CAG must confirm that the lesions of left main stenosis is higher than 30%, or coronary artery stenosis of higher than 50% exists at either anterior descending artery or circumflex artery or right coronary artery or there was a clear diagnosis of myocardial infarction. To be part of the control group, his or her CAG must confirm that there were no atherosclerotic lesions in any of the four major vessels (left main trunk, anterior descending branch, circumflex artery and right coronary artery) or the patient has suffered acute myocardial infarction (AMI) excluded by ECG, echocardiography and myocardial enzymology check.

The detailed health histories of all participants and the high risk factors of coronary diseases including gender, age, smoking, history of hypertension, diabetes, hyperlipidemia, obesity, etc. have been recorded. Hypertension was diagnosed by historic records or more than two clinical examinations showing the systolic blood pressure exceeding 140 mmHg or the diastolic blood pressure being greater than 90 mmHg. Diabetes mellitus were diagnosed by a known history, or criterions set by American Diabetes Association.[8] Hyperlipidemia was defined as triglyceride levels being higher than 1.8 mmol/L, or total cholesterol levels being higher than 5.2 mmol/L by laboratory examination. Individuals who have smoked two cigarettes or more daily for more than one year were classified as smokers. Body mass index (BMI) was calculated by dividing weight in kilogram by square of height in meters and defined as being increased when it is over 25 kg/m^2.

This study is incompliance with the regulations of Beijing Anzhen Hospital Ethics Committee with written consent of acknowledgment from all participants.

2.2 Biochemical investigation

Venous blood sample was drawn after an overnight fasting. Serum total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglyceride (TG) and blood glucose were measured with automated enzymatic methods by Olympus-1000 Automated Analyzer (Tokyo, Japan) following all manufacturer's instructions.

2.3 Genotype determination

Venous blood from all individuals in the study was col-

lected in vials containing EDTA. The samples were stored at −80°C until the extraction of DNA. Genomic DNA was extracted from peripheral blood leukocytes with QIAamp DNA Mini Kit (Quiagen, Germany). Primers were 5'-ACG TTGGATGTCCAAGTAGGTAGATGCTGG-3' (forward) and 5'-ACGTTGGATGTTGCCAAACTCAGCCTCTTG-3' (reverse) for rs2076185. The sequences of the primers and probes for each SNP are available on request. Genomic DNA (10 ng) and 0.5 μmol/L primer mix was used for each reaction. Amplification was set to perform 15 min of initial denaturation at 94°C, followed by 11 cycles of 94°C for 20 s, 56°C for 30 s, and 72°C for 1 min. Then the temperature is held at 72°C for 3 min with a final extension at 4°C for 5 min. Genotyping was done by matrix-assisted laser desorption ionization time of fight mass spectrometry (MALDI-TOF MS) using the MassARRAY system (Sequenom, San Diego, CA, USA), and analyzed using MassARRAY Tyer software (version pm4.0; Sequenom). Repeated analyses were done on 10% of randomly selected samples with high DNA quality for the quality control purpose.

2.4 Statistical analysis

The analysis of clinical characteristics was performed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). The continuous variables were expressed as means ± SD and tested with a two-sided *t*-test. The categorical variables were tested using the Pearson Chi-square test. Further statistical analysis was conducted in Plink 1.07 software. Hardy- Weinberg equilibrium (H-WE), genotype and allele frequencies were examined using the Pearson Chi-square test. An association analysis based on unconditional univariate logistic regression and multivariate logistic regression was carried out to determine the OR and 95% CI for two SNPs in three genetic models (dominant, recessive and additive). A two-side $P < 0.05$ was considered statistically significant.

3 Results

A total of 1382 subjects were included in this case-control study. The clinical characteristics of all the subjects are shown in Table 1. Compared with the control group, the age group of PCAD is lower than of the control group ($P = 0.001$). A majority of the patients in the pf PCAD group are male such that the occurrences of smoking, high fat disease history, diabetes prevalence rate are significantly higher ($P < 0.001$). The fasting blood glucose of the PCAD group increases significantly and the blood lipid level of HDL-C levels decreases significantly ($P < 0.0001$). The two groups are not statistically different on hypertension, BMI, TC, TG and LDL-C, ($P > 0.05$).

Table 1. Clinical characteristics of the study subjects.

	PCAD patients (n = 636)	Controls (n = 746)	*P*
Age, yrs	44.87 ± 6.18	46.23 ± 6.30	0.001
Gender, M/F	406/230	300/446	< 0.001
Smoking	325 (51.10)	200 (26.81)	< 0.001
BMI, kg/m^2	26.99 ± 3.47	26.59 ± 3.85	0.085
Hypertension	345 (54.25)	374 (48.95)	0.127
Diabetes	160 (25.16)	108 (14.48)	< 0.001
TC, mmol/L	4.54 ± 1.03	4.43 ± 1.20	0.135
Triglycerides, mmol/L	2.15 ± 1.72	1.94 ± 1.74	0.066
HDL-C, mmol/L	1.01 ± 0.27	1.09 ± 0.29	< 0.001
LDL-C, mmol/L	2.73 ± 0.85	2.70 ± 0.93	0.515

Data are expressed as mean ± SD or *n* (%) unless other indicated. BMI: body mass index; HDL-C: high density lipoprotein cholesterol; LDL-C: low density lipoprotein cholesterol; PCAD: premature coronary artery diseases group; TC: total cholesterol; TG: triglycerides.

In the control group, age, gender, history of hypertension, history of diabetes, smoking history, BMI, hyperlipidemia and lipid factors are influencing factors in the logistic regression analysis. Conditional logistic regression analysis of backward gradual statistics shows age, female gender, smoking, hypertension, diabetes, and hyperlipidemia are the main influencing factors ($P < 0.05$) of premature CHD, while the female is a protective factor with OR less than one (Table 2).

SNP genotypes were tested for deviation from H-WE for controls, and all polymorphisms were in H-WE. Table 3 shows the distribution of the rs2076185 genotypes of the PCAD group and the control group. The genotypes of rs2076185 were observed and the alleles were A and G. The frequencies of allele G of rs2076185 was 54.2% in the PCAD group and 49.5% in the control group. Significant statistical difference of the genotypes of the rs2076185 was observed between the PCAD group and the control with $\chi^2 = 6.337$ and $P = 0.042$. The allelic association of rs2076185

Table 2. Logistic regression analysis of the risk in the PCAD.

	OR (95% CI)	*P*
Age	1.033 (1.003–1.064)	0.027
Female	0.548 (0.212–0.363)	0.004
Smoking	2.099 (1.521–2.897)	< 0.001
Diabetes	1.822 (1.252–2.650)	0.002
Hypertension	1.299 (1.001–1.685)	0.049
Hyperlipemia	1.828 (1.032–2.942)	< 0.001

PCAD: premature coronary artery diseases group.

Table 3. The distribution of the rs2076185 genotypes.

Genotype	PCAD patients (n = 636)	Controls (n = 746)	χ^2	P
AA	131	186	6.337	0.042
AG	306	380		
GG	183	178		

PCAD: premature coronary artery diseases group.

in the PCAD group and the control group is shown in Table 4. Significant statistical difference was observed between the PCAD group and the control group in the allele G with OR of 0.828, 95% CI: 0.712–0.962 and $P = 0.014$.

The association of the rs2076185 with PCAD was analyzed using a logistic regression analysis by various models such as additive model (AA *vs*. AG *vs*. GG), dominant model [(AA+AG) *vs*. GG] and recessive model [AA *vs*. (AG+GG)]. The study started with the univariate analysis with rs2076185 and factors listed in Table 2 as variables. Table 4 shows that the rs2076185 polymorphisms were associated with the PCAD only in additive and dominant models. Subsequently, the analysis showed the factors in Table 2 were confounding variables of rs2076185 ($P < 0.05$). After removing these confounding variables, rs2076185 become associated with PCAD in all the three models as shown in Table 5.

4 Discussion

CHD is a complex, polygenic diseases caused by the interaction between multiple pathogenic factors and multiple micro-effect genes. The SNP of these susceptibility genes can be the genetic markers of susceptibility to CAD and contribute to the disease susceptibility and heterogeneity. Effects of environmental and genetic factors are different among individuals. Consequently, the genetic factors account for a greater portion for younger patients whereas the non-genetic factors such as environments play a more important role in the development of the disease process with the increasing age. Therefore, more attention is devoted to the study of genes in the early onset of CHD.

Table 4. Allelic association of rs2076185 in the PCAD group and the control group.

	PCAD patients	Controls
Number	636	746
Major (A)	568 (45.8%)	752 (50.5%)
Major (G)	672 (54.2%)	736 (49.5%)
OR (95% CI)	0.828 (0.712–0.962)	
P	0.014	

PCAD: premature coronary artery diseases group.

Table 5. Association of rs2076185 polymorphisms with PCAD in univariate and multivariate analyses.

	Univariate			Multivariate		
	OR	95% CI	P	OR	95% CI	P
Additive	0.828	0.711–0.964	0.015	0.775	0.648–0.928	0.005
Dominant	0.753	0.591–0.958	0.021	0.698	0.527–0.925	0.012
Recessive	0.802	0.622–1.034	0.089	0.804	0.538–0.983	0.038

Multivariate: adjustment for potential confounding variables (age, gender, smoking, diabetes and high density lipoprotein cholesterol). PCAD: premature coronary artery diseases group.

SNPs in the chromosome 6p24 closely related to CHD are mainly in the region of chromosome 6p24.1, where a c6orf105 genome with unclear function is found. The genome consists of ADTRP gene and PHACTR1 gene. Although SNP1252453 in PHACTR1 gene is strongly associated with CAD in Europeans and Americans, a query of the HapMap database shows that the minimum allele frequency (MAF) of this SNP in the Chinese Han population is 0. It's also found that the PHACRTR1 gene has nothing to do with the occurrence of CAD in Chinese Han population after 113 SNPs of PHACTR1 gene have been studied in GWAS of Chinese Han population. Therefore, the gene segment in Chromosome 6p24.1 associated with CAD may reside in gene ADTRP. The rs2076185 discovered in the study is located in the exon-missense area of the ADTRP gene. Exon-missense means that the codon encoding an amino acid changes into the codon encoding another amino acid due to a change of base pairs, resulting in the change of one of the hundreds of thousands of amino acid in proteins. The polypeptide chain loses its original function and is interpreted as different amino acid when formulating peptide. Thus, the protein spatial structure and biological function are affected. The missense mutation causes the generic mutation. The frequency difference between the case group and the control group in the genotype and allele analysis is statistically significant at site rs20676185. In subsequent logistic regression analysis, the site was associated with PCHD in the additive, dominant and hidden shape genetic models. Therefore, this site is very likely the genetic marker.

Study on c6orf105 generic group is still at the early phase. The function of c6orf105 and its impacts to CAD are unclear, needing further investigation. It is known that c6orf105 contains six exons, covering 65kb genomic regions and is expressed not only in the human heart, stomach, skin and kidneys, but also in vascular endothelial cells, monocytes, lymphocytes and HeLa and HepG2 cells.[3] The expression of c6orf105 gene in the lymphocytes of CHD patients was significantly lower than that of the normal control group.[8,9] The protein encoded by c6orf105/ADTRP regulates tissue factor pathway inhibitor (TFPI) mRNA ex-

pression and cell-associated anticoagulant activity of TFPI response to androgen.[3,8] SNP rs6903956 found in Chinese Han population previously was located within the ADTRP and proved to be highly sensitive to CHD. It suggests that the decreased expression of c6orf105 may be involved in the pathogenesis of CHD. Therefore, inferring that rs6903956 may affect the risk of CHD by influencing the expression of c6orf105 mRNA, ADTRP is considered to be the protective factor of CAD.[5] The ADTRP gene was first identified to be in association with CHD in the Chinese Han population and was further confirmed in the Han population in Singapore and the Japanese population.[5,6] However, the study of the above two groups of population have been focused on rs6903956. No new generic loci associated with CAD have been located.

The understanding of the function and structure of c6orf105 has been limited so far. The bioinformatics analysis on c6orf105 showed that the gene is conservative across species with higher homology. The gene sequence comparison found that it consisted of a conservative male hormone-induced domain (AIG1) and six transmembrane domains. Similar to what Lupu, *et al*.[8] found and published in the 52nd Annual Meeting of the American Hematology, our preliminary hormone-induced experiments shows that the androgen can increase c6orf105 HUVEC expression, suggesting androgens may have agonist-like effect on the gene. At the same time, we have also found that the decreased expression of c6orf105 is associated with gene mutation and the risk of CHD in Chinese population as well.[3] In addition, c6orf105 encoded protein may participate in the process of coagulation, resulting in the close relationship between c6orf105 gene and endothelial cell injury and apoptosis and endothelial-monocyte adhesion to protect the endothelial cells and strengthen the anticoagulant effect. This may be one of the important mechanisms of c6orf105 genes affecting CHD.[8]

In 2015, Chinetti-Gbaguidi G, *et al.*[10] of the Research Institute of France Diabetic Genome published a study on the c6orf105 expression in human macrophages and atherosclerotic lesions. They found that c6orf105 is expressed by recycled mononuclear cells and exists in human atherosclerotic plaque macrophages. Compared with healthy tissues, the expression level of c6orf105 gene in the area of atherosclerosis is increased significantly. Another interesting disclosure was the level of c6orf105 gene expression and atherosclerotic lesions in the macrophage marker CD68 are correlated positively, suggesting that macrophages are the main source of c6orf105 in atherosclerotic tissues. Further, an immunohistochemistry study also confirmed that c6orf105 is expressed by the macrophages in human atherosclerotic tissues. In the study of human atherosclerotic tissues, it is also found that the expression of c6orf105 was related to the activation of peroxisome proliferator-activated receptor (PPAR) γ. This transcription factor of such a similar PPAR family plays an important role in the regulation of macrophage gene expression and function realization. Association analysis revealed that the expression of c6orf105 gene was associated with the expression level of the three members of the PPAR family. The increasing PPAR γ was associated with the expression of c6orf105 in human macrophages and atherosclerotic lesions.[11] The macrophages played an important role in the pathophysiology of atherosclerosis by controlling the inflammatory response and lipid metabolism. The activation of PPAR increases the expression of c6orf105 in human macrophages. Macrophages have presented different phenotype in different microenvironments.[12] However, through the massive observation of M1 macrophages, c6orf105 expression level was not affected by the macrophage polarization state, and the activation of PPAR γ induces the expression of c6orf105 gene in all subtypes of the macrophages since c6orf105 has 51% homology with human-androgen-induced 1 gene.[10] PPAR γ ligands may induce the secretion of tissue factor pathway inhibitor (TFPI) in human macrophages and endothelial cells,[13] further elaborating the relationship between c6orf105 gene and atherosclerosis at the molecular biology level. Besides, Chinetti-Gbaguidi, *et al.*[10] also noticed that the expression of c6orf105 gene in the circulating blood monocytes of the obese diabetic subgroup had decreased significantly when compared with lean diabetes subgroup while the risk of CHD in this subgroup has increased significantly in the European Caucasian populations. However, no association of s6903956 with CHD was found in the previous GWAS study of the European Caucasian populations. There may be other SNP involved in the pathogenesis of CHD in addition to rs6903956 SNP.

The HapMap database shows that the MAF varies widely among different ethnic groups. For examples, MAF of rs6903956 is 5.6% in the Chinese Han population, 6.7% in the Japanese population, 28.0% in European Caucasian population, and 31.7% in African populations.[5] Although MAF of rs6903956 in European Caucasian population is much higher than that of Chinese Han population, GWAS was not found in Caucasian populations, indicating that the relationship between rs6903956 SNP and CHD may be limited only within the Chinese Han population and can be caused by several reasons. Each population has its specific structure with different genetic modification gene.[15] The interactions between genes-genes and between gene-environment can be different.[16,17] Interactions among disease

susceptibility genes and between disease susceptibility genes and environments are critical to the disease susceptibility. The classic GWAS study has been focused on the association of a SNP or a group of SNPs with diseases, but lacks consideration of potentially important disease-related genes in different sub-groups of a population.[18] Different populations have different lifestyles with different exposure risk factors. The founder effect can also contribute to it.[19,20] It's a kind of genetic drift referring to a new group re-established by a small number of individuals with parts of allelic genes within the parental population. Their genes are barely different because it has not breed with other groups of organisms though the population will grow later. There are tens of millions of human genome SNPs, but the studied chips only contain about 500,000 SNPs. The coverage is so insufficient that the SNP rs6903956 may be only a genetic marker. The actual CHD related pathogenic or functional SNPs may reside in the LD block highly linked with SNP rs6903956. But SNP rs2076185 of this study and rs6903956 are all located inside c6orf105 gene.

A recent study shows that old people are dominant in CAD patients though there is a tendency to have more and more young CAD patients. The *Report on Cardiovascular Diseases in China (2013)* suggested that there are 29 million CAD patients in China and the death ratio of CAD is 255 in every 100,000 patients in 2012 with 2 of 5 deaths caused by CAD.[21] The death ratio of myocardial infarction increases with the age exponentially with a significant increase starting at the age of 40, degrading the living quality of the patients.[21] The study of association of SNP with CAD has just started recently. By looking for the gene characteristics associated with CAD, the treatment of CAD can be more specific and selective, making the treatment safer and more effective; reducing the side effects of medication due to the physical differences of people; promoting personal preventions; decreasing the ratios of sickness or death of old people, thus improving their living quality. In order to study the Genetics, populations of PCAD were selected in this study. Whether the outcome of this study is applicable to old people shall be validated in future studies.

It is, however, the first time to report that the PCHD-related SNP rs2076185 is located in the missense mutation area of ADTRP gene. The HapMap database shows that the MAF of rs2076185 varies widely among different ethnic groups: 46.7% in Chinese Han population, 36.4% in the Japanese population and 6.7% in European Caucasian and African populations. Such differences among races may be the reason that rs2076185 is found to be associated with the occurrence of CHD rates in Chinese Han population. Whether SNP rs2076185 is associated with CAD in populations in racial groups other than Chinese Han population needs further investigation. Limited by the data sourcing from a single hospital, and patients mainly from northern China, the samples may not representative of the entire Chinese Han population. The sample size of 636 CAD cases *vs.* 746 control cases is low due to the limited sampling period. A further study will be conducted on expanding the sampling geographic region to have more complete coverage of China Han population. Study of mRNA sequencing of larger populations in subsequent study can help in detecting whether the affected population carries the mutated gene, thus validating the results of this paper and providing better insight into explaining the influencing mechanism of SNP rs2076185 to PCAD.

In conclusion, the SNP rs2076185 within the ADTRP gene on chromosome 6p24.1 was significantly associated with PCAD in univariate and multivariate analysis in Chinese Han population.

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