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Original Article

Relationship between rs11206510 and susceptibility, risk factors, and clinical characteristics of acute myocardial infarction in a Chinese Han population

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Abstract: The rs11206510 SNP has been confirmed to be related to acute myocardial infarction (AMI). The present study was undertaken to detect associations between rs11206510 and susceptibility, risk factors, clinical characteristics, and gene-environment interactions for AMI. In 600 Chinese Han patients, genotyping of rs11206510 SNPs was performed using polymerase chain reaction and restriction fragment length polymorphism. Significant differences in both genotypic and allelic frequencies of rs11206510 between the AMI group and the control group were detected ($P < 0.007$ for each). Interactions were found between subjects with TT genotype and smoking or alcohol consumption ($P < 0.001$). The mutant TC and CC genotypes and minor C allele of rs11206510 were positively correlated with increased risk of AMI. Also, interactions between the TT genotype of rs11206510 and smoking or alcohol consumption appear to increase the risk of AMI.

Keywords: Acute myocardial infarction, single nucleotide polymorphism, susceptibility, risk factor, clinical feature, gene-environment interaction

Introduction

Acute myocardial infarction (AMI) is caused by atherosclerotic coronary artery plaque erosion or ruptures, which lead to transient, partial, or complete arterial occlusion. AMI is one of the most serious types of coronary artery disease (CAD), with high fatality rates [1]. It is characterized by elevated ST segments in the reflecting leads and elevated levels of cardiac enzymes. In the United States, about 1.5 million people suffer from an AMI each year, reflecting an incidence of 66/100,000 per year. The data are similar among European countries, such as the Czech Republic, Belgium, and so on [2, 3]. In China, more than 8 million people per year suffer from AMI, and this number has been predicted to rise to up to 23 million people by 2030 [4]. AMI has become one of the most serious human diseases, resulting in a heavy medical and financial burden as well as seriously affecting quality of life. It is well established that AMI is a complex trait caused by multiple environmental and genetic factors and their interactions [5]. In 2009, 10 loci associated with AMI, including the rs11206510 single nucleotide polymorphism (SNP), were identified by the Myocardial Infarction Genetics Consortium [6]. One report from Iranian populations showed that homozygote genotypes for the rs11206510 SNP had a strong protective effect against CAD [7]. To our knowledge, however, the association between rs11206510 and AMI has not been previously reported in the Chinese Han population. Therefore, the present study was undertaken to evaluate whether the rs11206510 SNP and its interaction with environmental factors was related to susceptibility to, risk factors for, and clinical characteristics of AMI in this population.

Materials and methods

Study population

A total of 300 AMI patients and 300 healthy subjects who were matched for age, lifestyle,

and socioeconomic status, all in Guangxi province, People's Republic of China, were enrolled in the study from January 1, 2012 to December 31, 2014. The AMI patients consisted of 228 (76.0%) males and 72 (24.0%) females, ranging in age from 33 to 84 years, with a mean age of 61.67±10.43 years. The healthy control subjects consisted of 210 (70.0%) males and 90 (30.0%) females, aged 34 to 83 years, with a mean age of 58.49±10.54 years. The present study was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University, Guangxi province, People's Republic of China. Informed consent was obtained from all subjects after they received a full explanation of the study.

Subgroups

To assess the relationship between rs11206510 and clinical characteristics, the 300 cases comprising the AMI group were subdivided as follows. (1) They were subdivided into two subgroups on the basis of symptoms: those with typical symptoms (n = 78) and those with atypical symptoms (n = 222). (2) They were subdivided into four subgroups according to diagnosis time (DT): DT ≤ 2 h (n = 40); 2 h < DT ≤ 6 h (n = 119); 6 h < DT ≤ 12 h (n = 116); and DT > 12 h (n = 25). (3) They were subdivided into six subgroups according to infarction location: extensive anterior wall (n = 141), inferior wall (n = 97), anteroseptal wall (n = 18), lateral wall (n = 7), right ventricle (n = 13), and multivessel lesion (n = 24). (4) They were divided into two subgroups according to whether or not serious complications developed: no serious complications (n = 275) and serious complications (n = 25).

Epidemiological survey

Information on demographics, socioeconomic status, and lifestyle factors was collected using standardized questionnaires. Information on alcohol consumption included questions about the number of liangs (about 50 g) of rice wine, corn wine, rum, beer, or liquor consumed during the preceding 12 months. Alcohol consumption was categorized into groups according to grams of alcohol consumed per day: ≤ 250 g and > 250 g. Smoking status was categorized into groups according to cigarettes smoked per day: ≤ 20 and > 20. Height, weight, and waist circumference were manually measured under the supervision of two people. Sitting blood pressure was measured three times, using a mercury sphygmomanometer, separated by 15-minute rest intervals, and the average of the three measurements was used as the blood pressure measurement. Body mass index (BMI) was calculated as weight in kg divided by the square of height in meters (kg/m^2).

Biochemical analysis

The survey was carried out using internationally standardized methods [8]. Serum total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), creatine kinase-MB (CK-MB), and cardiac troponin I (cTnI) levels were obtained from samples analyzed by the biochemical laboratory of the First Affiliated Hospital, Guangxi Medical University, Guangxi province, China.

DNA amplification and genotyping

Genomic DNA was extracted from peripheral blood leukocytes using the phenol-chloroform method [9]. The extracted DNA was stored at 4°C for future analysis. Genotyping of the rs11206510 SNP was performed using the following primer pair: sense primer 5'-GTTGCTGCCTTGCTTCCTATT-3', anti-sense primer 5'-CCAGGAGGAGGAAGTGACCAA-3' (Sangon, Shanghai, People's Republic of China). Each 20 μL PCR reaction mixture consisted of 1.0 μL of genomic DNA, 0.8 μL of each primer (10 pmol/L), 10 μL of 2X *Taq* PCR Mastermix (20 mM Tris-HCl, pH 8.3, 100 mM KCl, 3 mM $MgCl_2$, 0.1 U *Taq* polymerase/μL, 500 μM of each dNTP), and 8 μL of ddH_2O (DNase/RNase-free). The reaction mixture was subjected to denaturation at 95°C for 5 min, followed by 35 cycles at 95°C for 30 s, 63°C for 30 s, and 72°C for 30 s, followed by a final extension at 72°C for 7 min. Then, the amplification products, in 5 mL CutSmart® Buffer, were digested using 5 U of *BtgZI* restriction enzyme (New England Biolabs, Inc, Beverly, MA, USA) at 37°C overnight. After restriction enzyme digestion of the amplified DNA, genotypes were identified by electrophoresis on ethidium bromide-stained 2% agarose gels and visualized with ultraviolet illumination. Genotypes were scored by an experienced reader blinded to epidemiological data and serum lipid levels. Six samples (genotypes: 2 TT, 2 TC, and 2 CC) that were positive by PCR-

Table 1. General characteristics and serum lipid levels of AMI and control groups

Parameter	AMI group	Control group	t (x^2)	P
Number	300	300	-	-
Male/female	228/72	210/90	2.740	0.098
Age (years)	61.67±10.43	58.49±10.54	3.712	< 0.001
Body mass index (kg/m^2)	23.76±3.11	22.66±3.15	4.296	< 0.001
Cigarette smoking [n (%)]	-	-	69.924	< 0.001
Nonsmoker	156 (52.00)	225 (75.00)	-	-
≤ 20 cigarettes/day	61 (20.33)	65 (21.67)	-	-
> 20 cigarettes/day	83 (27.67)	10 (3.33)	-	-
Alcohol consumption [n (%)]	-	-	42.887	< 0.001
Nondrinker	226 (75.33)	240 (80.00)	-	-
≤ 25 g/day	26 (8.67)	54 (18.00)	-	-
> 25 g/day	48 (16.00	6 (2.00)	-	-
Total cholesterol (mmol/L)	5.20±0.95	4.97±1.05	2.775	0.006
Triglycerides (mmol/L)	1.66±1.13	1.45±1.11	2.217	0.027
LDL-C (mmol/L)	3.71±0.92	2.89±0.87	11.241	< 0.001
HDL-C (mmol/L)	1.08±0.26	1.36±0.25	-13.176	< 0.001

HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

RFLP were also confirmed by direct sequencing. The PCR products were purified by low melting point gel electrophoresis and phenol extraction, and sequenced by Shanghai Sangon Biological Engineering Technology & Services Co., Ltd., People's Republic of China.

Diagnostic criteria

The diagnostic criteria and study protocol followed the guidelines of the European Resuscitation Council [10-12]. Inclusion in the study required a diagnosis of ST-segment elevation myocardial infarction (STEMI), defined as follows: a 12-lead electrocardiogram showing ST-segment elevation of 1 mm or greater in at least two contiguous leads; prolonged chest discomfort typical of myocardial ischemia; cardiac biomarkers, and creatine kinase-MB (CK-MB) or troponin (or both) elevated to more than twice the upper limit of normal laboratory reference values; with coronary artery radiography confirmation. Ventricular fibrillation (VF) was defined on the basis of the following atypical electrocardiogram patterns: chaotic irregular deflections of varying amplitude; no identifiable P waves, QRS complexes, or T waves; and heart rate between 150 and 500 beats/min. Shock was defined as systolic blood pressure < 90 mm Hg; high heart rate (> 120 beats/min); pale and clammy skin; and confusion. Heart failure (HF) diagnosis was determined on the basis of brain natriuretic peptide (BNP) and heart ultrasound. The normal values of serum TC, TG, HDL-C, LDL-C, CK-MB, and cTnI in our Clinical Science Experiment Center were 3.10 - 5.17 mmol/L, 0.56 - 1.70 mmol/L, 0.91 - 1.81 mmol/L, 2.70 - 3.20 mmol/L, 0 - 25 mmol/L, and 0 - 0.014 ng/mL, respectively. Hypertension was diagnosed according to the criteria of the 2003 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension [13]. Normal weight, overweight, and obesity were defined as BMI 19 - 24, BMI 25 - 28 or > 28 kg/m^2, respectively [14].

Statistical analyses

All statistical analyses were carried out using the statistical software package SPSS 19.0 (SPSS Inc., Chicago, Illinois, USA). Conformity to the Hardy-Weinberg equilibrium was tested by the χ^2-test in controls. Qualitative variables were expressed as raw count and percentage. Mean ± standard deviation was used for the presentation of quantitative variables. Genotypic and allelic frequencies were calculated by direct counting. A chi-square analysis was used to evaluate the difference in genotype distribution and sex ratio between the groups. The difference in general characteristics between the AMI group and the control group was evaluated by Student's unpaired *t*-test. Sex, age, BMI, alcohol consumption, and cigarette smoking were adjusted for the statistical analysis. In order to characterize the impact of gene-environment interaction on AMI, the correlation between genotype and several environmental factors was evaluated by non-conditional binary logistic regression analysis with stepwise modeling. Odds ratios (ORs) and corresponding 95% confidence intervals (95% CI) were also calculated. After Bonferroni correction, a two-tailed *P* value less than 0.007 (*P* = 0.05/7, cor-

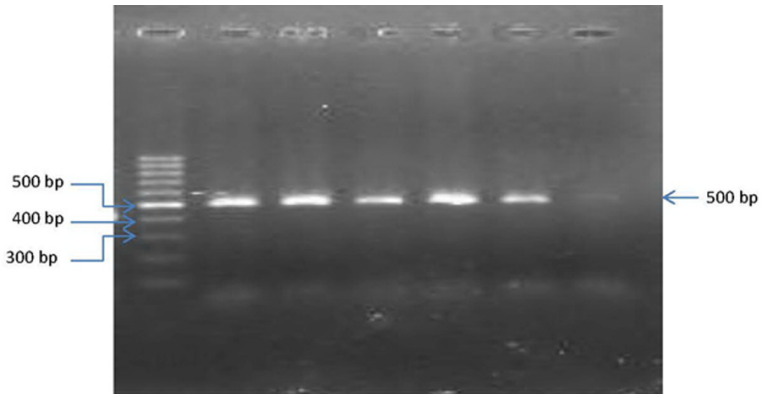

Figure 1. Electrophoresis of PCR products of the rs11206510 *PCSK9* gene variant.

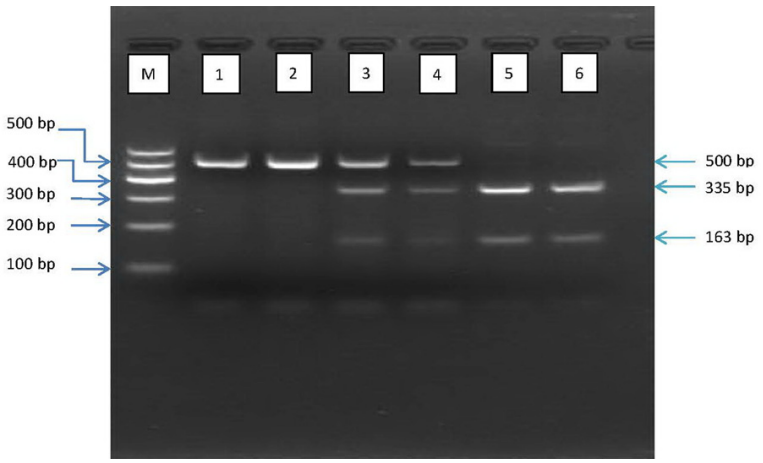

Figure 2. Genotyping of the rs11206510 polymorphism of the *PCSK9* gene. (Band 1 and 2: TT genotype, 500 bp; band 3 and 4: TC genotype, 500 bp, 335 bp and 165 bp; band 5 and 6: CC genotype, 335 bp and 165 bp).

responding to $P < 0.05$ after adjusting for 7 independent : rs11206510 SNPs and BMI, cigarette smoking , alcohol consumption, rs11206510- BMI, rs11206510- cigarette smoking and rs11206510- alcohol consumption) was considered statistically significant.

Results

General characteristics and serum lipid levels

Comparison of generalized features can be found in **Table 1**. Mean age (61.67±10.43 *vs.* 58.49±10.54) and BMI (23.76±3.11 *vs.* 22.66±3.15) were higher in the AMI group than in the control group. The numbers (percentages) of subjects who smoked and consumed alcohol at higher levels were 144 (48.00) and 74 (24.67%) in the AMI group, respectively, and 75 (25.00 %) and 60 (20.00%) in the control group, respectively. Significantly more subjects in the AMI group smoked and consumed alcohol at higher levels than in the control group ($P < 0.001$ for each). There were no significant difference in sex ratio between the two groups ($P > 0.007$).

Comparisons of lipid levels are also shown in **Table 1**. The levels of TC and LDL-C were 5.20±0.95 mmol/L and 3.71±0.92 mmol/L in the AMI group, respectively, and 4.97±1.05 mmol/L and 2.89±0.87 mmol/L in the control group, respectively. The levels of serum TC and LDL-C in the AMI group were significantly higher than those in the control group ($P < 0.007$ for each). However, the serum HDL-C level in the AMI group was lower than in the normal group (1.08±0.26 mmol/L vs. 1.36±0.25 mmol/L, $P < 0.001$). There was no significant difference in serum TG levels ($P > 0.007$).

Electrophoresis, genotyping, and sequencing

Amplification of genomic DNA yielded PCR products of 500 bp (**Figure 1**). The genotypes identified were named according to the presence (T allele) or absence (C allele) of the enzyme restriction sites. Thus, the TT genotype is a wild-type homozygote for the absence of the site (bands at 280 bp, lanes 1 and 2; **Figure 2**). The TC genotype is a heterozygote for the absence and presence of the site (bands at 500, 335, and 163 bp, lanes 3 and 4; **Figure 2**). The CC genotype is a homozygote for the presence of the mutated site (bands at 335 and 163 bp; lanes 5 and 6, **Figure 2**). The genotypes of TT, TC, and CC detected by the PCR-RFLP were also confirmed by sequencing (**Figure 3**).

Genotypic and allelic frequencies

There were no detectable deviations of genotypic frequencies from the Hardy-Weinberg equilibrium in control group. ($X^2 = 0.065$, $P >$

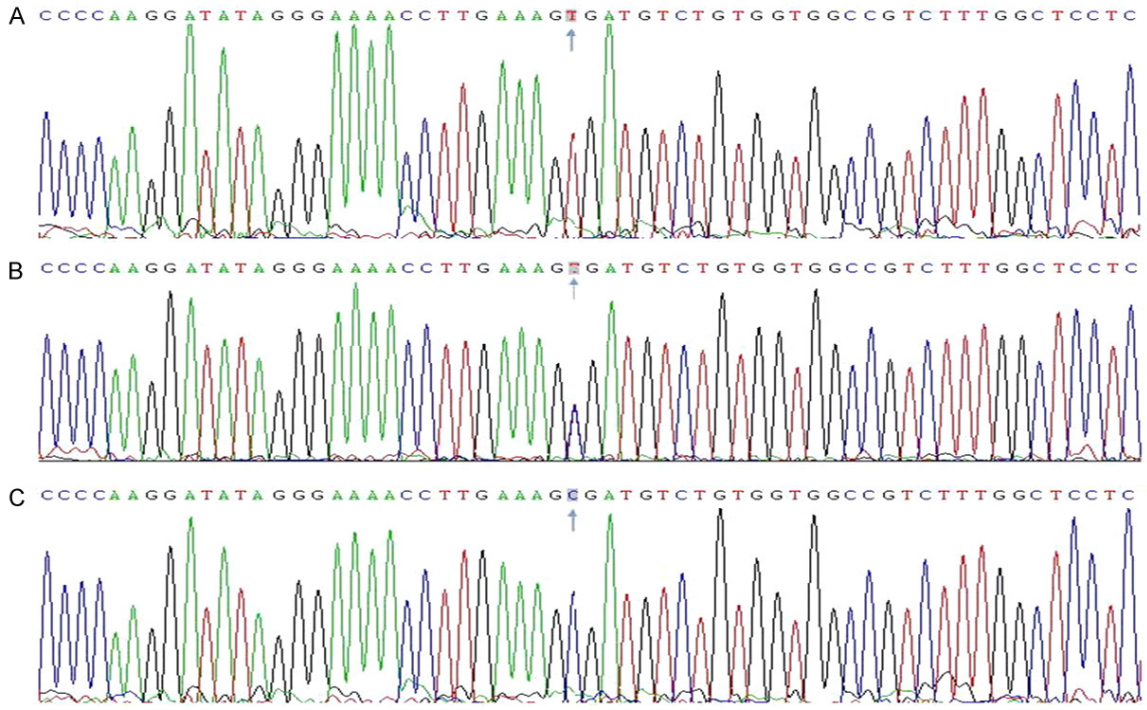

Figure 3. Partial rs11206510 nucleotide sequence from the *PCSK9* gene. (A: TT genotype; B: TC genotype; C: CC genotype).

Table 2. Differences in distribution of rs11206510 genotype and allele frequency between the AMI and control groups

Parameter	AMI group [n (%)]	Control group [n (%)]	X^2	*P*
Number (n = 600)	300 (50.00)	300 (50.00)	-	-
Genotypes	-	-	12.038	0.002
TT	239 (79.67)	262 (87.34)	-	-
TC	49 (16.33)	37 (12.33)	-	-
CC	12 (4.00)	1 (0.33)	-	-
Allele	-	-	11.384	0.001
T	527 (87.83)	561 (93.50)	-	-
C	73 (12.17)	39 (6.50)	-	-

0.007). The genotypic and allelic frequencies of rs11206510 SNPs are shown in **Table 2**. The wild-type TT genotype and T allele frequency, respectively, were 79.67% and 87.83% in the AMI group, which was significantly lower than those in the control group, 87.34% and 93.50% ($P < 0.007$). The frequencies of the TC and CC genotypes and the minor C allele were 16.33%, 4.00%, and 12.17%, respectively, in the AMI group. These values were significantly higher than those seen in the control group: 12.33%, 0.33%, and 6.50% for the TC, CC, and minor C alleles, respectively ($P < 0.007$).

Risk factors for AMI

As shown in **Table 3**, non-conditional binary logistic regression analysis showed that diabetes, high blood pressure, age and smoking were strongly associated with AMI risk, with OR values of 69.214, 9.080, 4.775, and 4.674, respectively ($P < 0.001$ for each). In contrast, HDL-C was negatively correlated with the risk of AMI, with an OR value of 0.052 ($P < 0.001$). However, no significant differences were seen between AMI and control groups in terms of correlation of sex, BMI, TC, TG, rs11206510 SNP, alcohol consumption, and LDL-C with the risk of AMI ($P > 0.007$ for each).

Frequencies of rs11206510 and clinical characteristics

There were no significant differences in the genotypic and allelic frequencies of rs11206510 between the controls and the AMI subgroups,

Table 3. Risk factor analysis by univariate logistic regression in AMI group (n = 300)

Parameter	B	SE	Wald	Sig	Exp (B)/OR
Diabetes	4.237	1.155	13.461	0.000	69.214
High blood pressure	2.206	0.362	37.086	0.000	9.080
Age	1.563	0.327	22.828	0.000	4.775
Smoking	1.542	0.250	38.038	0.000	4.674
HDL-C	-2.953	0.724	16.639	0.000	0.052
Sex	0.854	0.357	5.085	0.024	2.235
BMI	0.662	0.330	4.029	0.180	1.938
TC	0.989	0.530	3.488	0.248	2.689
TG	0.380	0.345	1.216	0.270	1.462
Rs11206510	0.344	0.354	0.943	0.331	1.410
Alcohol consumption	0.192	0.258	0.554	0.457	1.313
LDL-C	0.184	0.553	0.110	0.740	1.202

including subgroups divided according to diagnosis time, typical symptoms, serious complications, and infarction location ($P > 0.007$ for each) (**Table 4A-D**).

Interaction between rs11206510 and BMI, smoking, and alcohol consumption

In **Table 5**, as age, sex and serum lipid levels were adjusted, there were significant interactions between presence of the minor T allele and smoking or alcohol consumption ($P < 0.001$ for each). The subjects who smoked < 20 cigarettes/day or who smoked ≥ 20 cigarettes/day who also had the minor T allele had an increased risk for AMI of 1,276.5% and 946.3%, compared with subjects in the same smoking category who were heterozygous or homozygous for the C allele. For the subjects who had the minor T allele, those who consumed < 250 g/day of alcohol had a 962.8% increased risk for AMI while those who consumed ≥ 250 g/day of alcohol had a 1,469.2% increased risk for AMI. There was no interaction between presence of the minor T allele and BMI ($P > 0.007$). No interactions were seen between the TC and CC genotypes and BMI or smoking that significantly affected AMI risk ($P > 0.007$ for each).

Discussion

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is the ninth member of the subtilisin/kexin family of proprotein convertases. Genome-wide association studies (GWAS) have found that the common allele T of the *PCSK9* gene rs11206510 SNP on chromosome 1p32 was associated with both increased LDL-C and increased risk of coronary artery disease (CAD) in white populations [6]. In this study, we found that the mutant TC and CC genotypes and the minor C allele of the *PCSK9* rs11206510 SNP were positively correlated with AMI morbidity. At present, there is little information on the interaction between rs11206510 and AMI in Chinese populations. The mechanisms underlying the role of the *PCSK9* gene in elevated AMI risk involve control of LDL receptor (LDLR) protein levels, and consequently, blood LDL levels. PCSK9 accelerates the degradation of hepatic LDLR and inactivation of PCSK9 should theoretically decrease LDL levels [15-17]. Several PCSK9 loss-of-function mutations associated with low LDL cholesterol plasma levels have been described and variations in this gene decrease the risk of CAD [18]. Accordingly, it has been observed that African Americans who had a loss-of-function PCSK9 mutation leading to 40 mg/dL lower LDL-C had a 90% reduction in coronary events in their middle years [19]. The association of total and LDL cholesterol with the SNP rs11206510 has been replicated, with a significant association of the minor C-allele with lower concentrations of both LDL and total cholesterol in an Italian population [20].

A previous study verified that the MMP-9 genotype may influence the risk of clinical events in AMI patients [21]. However, in our study, there were no significant differences in the genotypic and allelic frequencies of rs11206510 between the controls and the AMI subgroups, including subgroups divided according to diagnosis time, typical symptoms, serious complications, and infarction location.

In the present study, we also assessed the association between SNP rs11206510 and several environmental factors. The data indicate that the interaction between the TT genotype of rs11206510 and higher smoking frequency or alcohol consumption level may result in an increased risk of AMI. Diabetes, high blood pressure, age, and smoking were all risk factors for AMI, while HDL-C was negatively correlated with AMI risk. AMI is a multifactorial disease with a complex pathogenesis, in which

Table 4A. Comparison of rs11206510 genotype and allele frequencies among different diagnosis time ranges in AMI group (n = 300)

Parameter	Groups [n (%)]				X^2	*P*
	DT ≤ 2 h	2 h < DT ≤ 6 h	6 h < DT ≤ 12 h	DT > 12 h		
Number (n = 300)	40 (13.33)	119 (39.67)	116 (38.67)	25 (8.33)	-	-
Genotype	-	-	-	-	16.424	0.037
TT	30 (75.00)	95 (79.83)	96 (82.76)	18 (72.00)	-	-
TC	8 (20. 00)	19 (15.97)	17 (14.64)	5 (20.00)	-	-
CC	2 (5.00)	5 (4.20)	3 (2.60)	2 (8.00)	-	-
Allele	-	-	-	-	3.295	0.348
T	68 (85.00)	209 (87.82)	209 (90.09)	41 (82.00)	-	-
C	12 (15.00)	29 (12.18)	23 (9.91)	9 (18.00)	-	-

Table 4B. Comparison of genotype and allele frequencies between the severe complications group and the non-severe complications group in AMI group (n = 300)

Parameter	Groups [n (%)]		X^2	P
	Complications	Non-complications		
Number (n = 300)	275 (91.67)	25 (8.3)	-	-
Genotype	-	-	0.002	0.999
TT	219 (79.64)	20 (80.00)	-	-
TC	45 (16.36)	4 (16.00)	-	-
CC	11 (4.00)	1 (4.00)	-	-
Allele	-	-	0.001	0.970
T	483 (87.82)	44 (88.00)	-	-
C	67 (12.18)	6 (12.00)	-	-

Table 4C. Comparison of genotype and allele frequencies between the typical symptoms group and the non-typical symptoms group

Parameter	Groups [n (%)]		X^2	P
	Typical symptoms	Non-typical symptoms		
Number (n = 300)	78 (26.00)	222 (74.00)	-	-
Genotype	-	-	0.567	0.753
TT	63 (80.77)	176 (79.28)	-	-
TC	13 (16.67)	36 (16.22)	-	-
CC	2 (2.56)	10 (4.50)	-	-
Allele	-	-	0.318	0.573
T	139 (89.10)	388 (87.39)	-	-
C	17 (10.90)	56 (12.61)	-	-

lifestyle, individual genetic background, and environmental risk factors are involved. Overwhelming evidence has confirmed that risk factors for AMI include high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol intake [22, 23]. However, little is known about the combined genetic influence of rs11206510 and environmental factors. Some recent studies have suggested telomere shortening as one factor [24]. Telomeres are specialised DNA-protein structures at the ends of all chromosomes, which preserve chromosome stability and integrity. In normal cells, the DNA replication machinery is unable to completely duplicate the telomeric DNA, and thus telomeres are shortened after each cell division [25]. Telomere length is highly variable at birth and decreases with age [26]. Previous studies have demonstrated an association between telomere length, health, and longevity [27]. Shorter leukocyte telomeres have been measured in MI cases and offspring of MI cases [28, 29]. Lifestyle is well known to be one of the stronger predictors of coronary heart disease (CHD) risk, and a modest effect of lifestyle on telomere length has been previously reported [30]. Smoking has been associated with shorter telomeres in normal-weight as well as in lean and obese women [31, 32], while greater physical activity in leisure time has been associated with longer telomeres in healthy twins [33]. Some previous studies have shown that subjects with impaired glucose tolerance and type II diabetes have shorter telomeres than controls [34, 35]. Another study demonstrated that men with lower vitamin C intake are more likely

Table 4D. Comparison of genotype and allele frequencies among different infarct sites

Parameter	Groups [n (%)]						X^2	*P*
	Extensive anterior	Inferior	Anteroseptal	lateral	Right ventricular	Multivessel lesion		
Number (n = 300)	141 (47.00)	97 (32.33)	18 (6.00)	7 (2.33)	13 (4.33)	24 (8.00)	-	-
Genotype	-	-	-	-	-	-	12.720	0.240
TT	111 (78.72)	78 (80.41)	16 (88.89)	7 (100.00)	11 (84.62)	16 (66.67)	-	-
TC	20 (14.19)	18 (18.56)	2 (11.11)	0 (0.00)	2 (15.38)	7 (29.17)	-	-
CC	10 (7.09)	1 (1.03)	0 (0.00)	0 (0.00)	0 (0.00)	1 (4.17)	-	-
Allele	-	-	-	-	-	-	7.546	0.183
T	242 (85.82)	174 (89.69)	34 (94.44)	14 (100.00)	24 (92.31)	39 (81.25)	-	-
C	40 (14.18)	20 (10.31)	2 (5.56)	0 (0.00)	2 (7.69)	9 (18.75)	-	-

Table 5. Interaction between rs11206510 genotypes and environmental factors and their impact on AMI (n-300)

Genotype	Environmental factor	B	SE	Wald	Sig	Exp (B)/OR	95.0% CI for OR	
							Lower	Upper
-	BMI (Kg/m^2)	-	-	-	-	-		
TT	19 - 24	-	-	3.588	0.058	-	-	-
TT	≥ 24	0.518	0.201	6.612	0.070	1.678	1.1131	2.490
TC+CC	19 - 24	-	-	0.014	0.907	-	-	-
TC+CC	≥ 24	1.280	0.519	6.090	0.098	3.597	1.301	9.943
-	Smoking (n/d)	-	-	-	-	-	-	-
TT	0	-	-	46.979	< 0.001	-	-	-
TT	0-20	2.547	0.372	46.925	< 0.001	12.765	6.160	26.453
TT	≥ 20	2.247	0.404	30.891	< 0.001	9.463	4.284	20.903
TC+CC	0	-	-	4.653	0.098	-	-	-
TC+CC	0-20	2.273	1.077	4.454	0.245	9.706	1.176	80.111
TX+XC	≥ 20	1.935	1.535	2.907	0.088	6.923	0.749	64.024
-	Alcohol (g/d)	-	-	-	-	-	-	-
TT	0	-	-	25.497	< 0.001	-	-	-
TT	0-250	2.265	0.485	21.844	< 0.001	9.628	3.725	24.888
TT	≥ 250	2.687	0.538	24.961	< 0.001	14.692	5.120	42.161
TC+CC	0	-	-	7.807	0.140	-	-	-
TC+CC	0-250	20.766	1.519E4	0.000	0.999	1.043E9	3.592	37.894
TC+CC	≥ 250	22.995	1.519E4	0.000	0.999	6.693 E9	6.505	138.364

to suffer from AMI [36]. Several environmental factors have been documented to influence biological mechanisms, but relatively little is known about gene-environment interaction effects. Further studies are essential.

Limitations

There were several limitations in the present study. First, the total number of patients in the study was small, which restricted the statistical power of our findings. Second, there was a lack of supporting materials between the gene and early diagnosis time. Finally, the study did not include any data shedding light on the mechanism underlying the association between the gene and AMI.

Conclusions

In conclusion, the data in the present study indicated that the mutant TC and CC genotypes and minor C allele of the *PCSK9* rs11206510 SNP were positively correlated with the risk of AMI. Also, the interaction between the minor T allele of rs11206510 and higher levels of

smoking or alcohol consumption, as well as the rs11206510 CC genotype and higher alcohol consumption, appear to increase the risk of AMI. Finally, it was once again verified that diabetes, high blood pressure, age, and smoking are risk factors for AMI, while HDL-C was negatively correlated with AMI risk.

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Disclosure of conflict of interest

None.

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