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Association of SNP rs17465637 with Acute Myocardial Infarction in the Chinese Han Population

Zhongyi Sun [1], Quanfang Chen [2], Zhou Huang [1], Dongling Huang [1], Tian Li [1], Fan Wang [1], Jun Li [1], Xuefeng Liu [1], Xiangtao Zeng [1], Qian Zeng [1], Guangxing Zhao [1], Haimei Yuan [1] and Wei Wang [1,*]

[1]Department of Emergency, the First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi, People's Republic of China
[2]Institute of Respiratory Disease, the First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi, People's Republic of China

[*]*Corresponding author*: Department of Emergency, the First Affiliated Hospital, Guangxi Medical University, Nanning, Guangxi, People's Republic of China. Email: weiwanggx@163.com

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Abstract

Background: Genome-wide association studies (GWAS) have recently shown that Single Nucleotide Polymorphism (SNP) rs17465637 on chromosome 1p41 is associated with atherothrombotic Coronary Artery Disease (CAD). However, whether rs17465637 acts as a protective factor or a risk factor for acute myocardial infarction (AMI) is not well understood in the general population.
Objectives: In this article, we aimed to determine whether this locus was related to susceptibility to AMI in a Chinese Han population.
Methods: A retrospective experimental study was performed in Guangxi province, People's Republic of China, on January 1, 2012, to December 31, 2017. We recruited 688 patients who were matched for age, lifestyle, and socioeconomic status from the Chinese Han population and subdivided them into two groups of 344 AMI patients and 344 healthy controls. We used standardized questionnaires to collect information on demographics, socioeconomic status, and lifestyle factors. Genotypes of SNP rs17465637 were determined by the TaqMan assay. Diagnostic criteria and research protocols were based on the guidelines of the European Resuscitation Commission. Statistical analysis was performed by SPSS version 22.0.
Results: The percentage of the AA genotype in the AMI group was 22.97%, which was greater than that of the control group (13.08%) (kappa = -0.082, $P < 0.001$). The AA genotype of SNP rs17465637 had significant differences between different infarct sites (kappa = -0.011, $P < 0.05$). There were interactions between the CC genotype and BMI $\geq$ 24 kg/m^2 (OR = 4.060, 95% CI = 1.680 - 9.812, P = 0.002) and smoking $\geq$ 20 cigarettes/d (OR = 2.732, 95% CI = 1.495 - 4.991, P = 0.001).
Conclusions: This study revealed that the AA genotype of SNP rs17465637 was positively correlated with the risk of AMI. Subjects with the AA genotype were positively correlated with extensive anterior of AMI. Also, interactions between the CC genotype of SNP rs17465637 and BMI or smoking seem to increase the risk of AMI.

Keywords: Chromosomes, Gene-Environment Interaction, Genome-Wide Association Study, Genotype, Myocardial Infarction, Protective Factors, Polymorphism, Risk Factors, Single Nucleotide, Susceptibility

1. Background

Coronary Artery Disease (CAD) is a complex disorder thought to be caused by both genetic and environmental factors and their interactions (1, 2). Acute Myocardial Infarction (AMI) has become the most serious disease, resulting in a heavy medical and financial burden and serious impacts on the quality of life (3). In the United States, AMI has about 1.5 million new cases each year, with an incidence of about 66/100,000 population, similar to that of European countries such as the Czech Republic, Belgium, etc. (4, 5). In China, more than 8 million people are living with AMI, and an estimated 23 million people will have AMI by 2030 (6). From the estates of the global burden of disease (GBD) study, the mortality rate of CAD in South Asia increased by 88%, while the global decline was 35% from 1990 to 2010 (7). The prevalence and mortality rates of South Asians are 40% to 180% higher than those of whites in relation to established risk factors and risk prediction equations (8, 9). In the absence of positive precautions, the number of people dying from CAD in South Asia is expected to increase by 50% by 2030 (10). In prospective studies in Trinidad and the UK, hereditary factors, high prevalence of insulin resistance, metabolic syndrome, and diabetes played critical roles in the risk of AMI, but they could not explain why the incidence of AMI increased in South Asia

(11). Nevertheless, in South Asia, only can one-third of high-risk Asians with CAD be explained by measured metabolic risk factors, suggesting that we need to search for genetic risk factors (9, 11).

Genome-Wide Association Studies (GWAS) provide a strategy for identifying genetic factors with common and complex features of the disease (12). In recent years, researchers have conducted several GWAS to map the shared susceptibility variants underlying CAD (13). These variants could be biomarkers themselves or point to circulating markers for further exploration. The Single Nucleotide Polymorphism (SNP) rs17465637, which is located on the gene MIA SH3 Domain ER Export Factor 3 (MIA3) and is in genetic disequilibrium, has been independently confirmed to be related to AMI in Japanese (14), European Origin (15), Pakistani (16), Siberian (17), and American Caucasian (18) populations. Genetic variants related to AMI in Chinese Han populations have not been definitively identified. Therefore, our investigation assessed whether SNP rs17465637 was involved in the susceptibility, risk factors, and/or clinical characteristics of AMI in the Chinese Han population.

2. Objectives

In this article, we aimed to determine whether this locus was related to susceptibility to acute myocardial infarction (AMI) in a Chinese Han population.

3. Methods

3.1. Study Population

A retrospective experimental study was performed in Guangxi province, People's Republic of China, from January 1, 2012, to December 31, 2017. The patients were matched for age, lifestyle, and socioeconomic status. According to the inclusion and exclusion criteria of the IABP-SHOCK II trial (19), patients were eligible for the trial if they had AMI. Patients were not eligible for the study if they did not have intrinsic cardiac action, were in coma with fixed dilatation of the pupils not induced by the drug, had been resuscitated for more than 30 minutes, had a mechanical cause of cardiogenic shock (e.g., ventricular septal defect or papillary muscle rupture), had shock more than 12 hours before screening, had a massive pulmonary embolism, severe peripheral arterial disease preventing the insertion of an intra-aortic balloon pump or aortic regurgitation with the severity of greater than grade II (on a scale of I to IV; upper grades indicating greater regurgitation), were over 90-years-old, were in a state of shock due to a condition other than AMI, or had a serious concomitant illness associated with a life expectancy of less than 6 months. Patients with incomplete information or unclear TaqMan assay results were also not eligible. Therefore, 344 patients in the control and experimental groups were selected from among 880 patients. The AMI patient group consisted of 266 (77.33%) men and 78 (22.67%) women, aged 33 - 84 years, with a mean age of 61.61 ± 10.73 years. Healthy controls comprised 238 (69.19%) males and 106 (30.81%) females aged 32 to 83 years, with an average age of 57.86 ± 10.86 years. The study was carried out following the principles of the Declaration of Helsinki. Written informed consent was not obtained and was not needed by the local law, as only anonymity patient data were used. The study was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University, Guangxi province, People's Republic of China, on November 16, 2011 (code: 2011-11-16). The author designed the study, collected and analyzed the data, analyzed and secured the data, drafted the manuscript, and agreed to publish it. Three employees from the institution of myocardial infarction of Guangxi medical university independently analyzed the data using SPSS 22.0 software. All subjects were enrolled after receiving a full explanation of the study.

3.2. Subgroups

To evaluate the relationship between SNP rs17465637 and clinical characteristics, 344 cases of the AMI group were subdivided as follows: (1) They were divided into two subgroups based on symptoms including those with typical symptoms (n = 86) and those with atypical symptoms (n = 258); (2) They were subdivided into four subgroups according to diagnosis time (DT) including DT $\leq$ 2 h (n = 58), 2 h < DT $\leq$ 6 h (n = 121), 6 h < DT $\leq$ 12 h (n = 114), and DT > 12 h (n = 51); (3) They were subdivided into six subgroups according to infarction location including extensive anterior wall (n = 182), inferior wall (n = 118), anteroseptal wall (n = 23), lateral wall (n = 7), right ventricle (n = 13), and multivessel lesion (n = 1); (4) They were divided into two subgroups according to whether or not serious complications developed, including no serious complications (n = 294) and serious complications (n = 50).

3.3. Epidemiological Survey

We used standardized questionnaires to obtain information on demographics, socioeconomic status, and lifestyle factors. Information on alcohol consumption included questions about the number of liangs (about 50 g) of corn wine, rice wine, beer, rum or alcohol consumed in the last year. The consumption of alcohol was grouped together according to grams of alcohol consumed per day:

< 250 g and ≥ 250 g. Smoking status was categorized into two groups on the basis of the number of cigarettes, < 20 and ≥ 20, smoked per day. Height, weight, and waist circumference were measured manually under the supervision of two people. Blood pressure was measured three times with a blood pressure monitor, the interval of the rest was 15 minutes and the average of three measurements was used as a measure of blood pressure. The body mass index (BMI) was the weight (kg) divided by square of height in meters (kg/m^2).

3.4. Biochemical Analysis

The survey was conducted using international standard methods (20, 21). Serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were measured and analyzed using a fully automatic biochemical analyzer (Itachi I7020, Itachi, Tokyo, Japan). The reagents were from Nanjing Perlong Biotechnology (Co., Ltd, Nanjing, China). CK-MB was evaluated using a kit from Human Biochemistry (Co., Ltd, Hessen, Germany) and cTnI was measured using a chemiluminescence apparatus. The supplementary reagents and reference substances were from Abbott (Abbott Park, IL, USA). All equipment had been calibrated by researchers beforehand. All data were available from the biochemistry laboratory of the First Affiliated Hospital, Guangxi Medical University, Guangxi province, China.

3.5. DNA Amplification and Genotypic

We perform a TaqMan test to confirm the genotypes of the whole blood samples (22). We amplified the genome of all samples using the AceQ® qPCR Probe Master Mix (Vazyme-innovation in enzyme technology, Nanjing, China). We utilized qTOWERE2.2 (Analytik Jena AG, Germany) to examine allelic discrimination. All equipment had been adjusted by researchers beforehand. Genotyping of SNP rs17465637 was carried out using the following primer pair: sense primer 5' - CACAGAACCAAACCATATCACTTTTTAA - 3', anti-sense primer 5' - TCAGCAGCAAAGACATGTTATCTTG - 3' (Nanning Guotuo Science and Technology Ltd.). The final volume of each reaction was 20 μL, containing 10 μL AceQ® qPCR Probe Master Mix (Vazyme-innovation in enzyme technology, Nanjing, China), 0.4 μL TaqMan probe mix, 2 μL Template DNA, 6.8 μL ddH20, 0.4 μL forward primer, and 0.4 μL reverse primer. The real-time PCR step consisted of an initial activation step of 5 min at 95°C, followed by 40 cycles of DNA fusion, an extraction and extension step of 15 min from sample at 95°C 15 s, 53°C 20 s, and at 72°C 7 min. Two researchers independently performed blind genotypic tests. In addition, our lab technicians randomly selected and analyzed approximately 10% of the samples to assure their quality. The agreement rate was 100%.

3.6. Diagnostic Criteria

Diagnostic criteria and research protocols were based on the guidelines of the European Resuscitation Commission (23-25). In our study, ST-elevation myocardial infarction (STEMI) was defined as follows: the 12-lead ECG showing ST elevation of at least two consecutive leads of at least 1 mm; typical myocardial ischemia with long-term chest discomfort cardiac biomarkers, and creatine kinase-MB (CK-MB) or troponin (or both) of more than twice the upper limit of normal laboratory reference values; coronary angiography was confirmed. Ventricular fibrillation (VF) was determined based on the following typical electrocardiogram patterns: irregular, chaotic deviations of varying amplitude; no P waves, QRS complexes or identifiable T waves; and heart rate of between 150 and 500 beats/min. The shock was defined as systolic blood pressure of < 90 mmHg, high heart rate (> 120 beats/min), pale skin, damp cold, and coma. Heart failure was determined by brain natriuretic peptide (BNP) and echocardiography. Normal values of TG, TC, HDL-C, LDL-C, CK-MB, and cTnI in the Clinical Science Experiment Center were 0.56 - 1.70 mmol/L, 3.10 ~ 5.17 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. The 2003 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension were used as the criteria for the diagnosis of hypertension (26). Normal weight, overweight, and obesity were defined as BMI of 19 - 24, BMI of 25 - 28, and > 28 kg/m^2, respectively (27).

3.7. Statistical Analyses

Statistical analysis was performed using the IBM SPSS Statistics Software, version 22.0 (IBM Corp., Armonk, Ill, USA). Hardy-Weinberg equilibrium conformance was tested by the χ^2-test on controls. Qualitative variables were expressed in raw numbers and percentages. The mean ± standard deviation was used to present the quantitative variables. Genotype and allele frequencies were calculated by direct counting. The χ^2-test was used to assess differences in genotype distribution and sex ratio between groups. The difference in general characteristics between the AMI group and the control group was evaluated by the Student's unpaired *t*-test. Risk factors and gene-environment interactions correlated with AMI were assessed by unconditional binary logistic regression analysis. The statistical analysis was adjusted to control for age, sex, BMI, cigarette smoking, and alcohol consumption. The

odds ratio (OR) and corresponding 95% confidence interval (95% CI) were also calculated. Bilateral P < 0.05 was considered statistically significant. When we estimated the interactions between SNP rs17465637 and smoking, BMI, and alcohol consumption, we considered bilateral P values of less than 0.007 (P = 0.05/7, corresponding to P < 0.05 after adjusting for seven independent factors: SNP rs17465637, BMI, cigarette smoking, alcohol consumption, rs17465637-BMI, rs17465637- cigarette smoking, and rs17465637-alcohol consumption) as statistically significant after Bonferroni correction.

4. Results

4.1. General Characteristics and Lipid Levels

As shown in Table 1, the mean age and BMI were higher in the AMI group than in the control group (61.61 ± 10.73 and 23.76 ± 3.47 vs. 57.86 ± 10.86 and 22.49 ± 3.14, P < 0.05 for both). The numbers (percentages) of subjects who smoked and drank alcohol were higher in the AMI group than in the control group [174 (50.60%) and 73 (24.13%) vs. 84 (24.40%) and 64 (18.60%); P < 0.05 for both]. There were also significant differences in the sex ratio between the two groups (χ^2 = -2.410, P < 0.05). TC and TG levels were higher in the AMI group than in the control group (4.56 ± 1.25 mmol/L vs. 4.25 ± 0.89 mmol/L; 1.64 ± 1.09 mmol/L vs. 1.40 ± 1.05 mmol/L, P < 0.05 for both). However, the serum HDL-C levels were lower in the AMI group than in the control group (1.13 ± 0.33 mmol/L vs. 1.70 ± 0.40 mmol/L, P < 0.001). There were no significant differences in serum LDL-C levels (2.72 ± 0.99 mmol/L vs. 2.84 ± 0.84 mmol/L, P > 0.05).

4.2. Genotypic and Allelic Frequencies

There were no detectable deviations of genotypic frequencies from Hardy-Weinberg equilibrium in the control group (χ^2 = 0.191, P = 0.662). As shown in Table 2, the percentage of the AA genotype in the AMI group was 22.97%, which was greater than that of the control group as 13.08% (kappa = -0.082, P < 0.001), while no difference was observed between the AMI group and the control group in the frequency of the A allele (kappa = -0.033, P > 0.05).

4.3. Risk Factors for AMI

As shown in Table 3, non-conditional binary logistic regression analysis showed that diabetes, high blood pressure, BMI, rs17465637, sex, TC, age, and smoking were strongly associated with the AMI risk, with OR values of 69.087, 15.436, 1.733, 1.408, 2.055, 2.547, 1.906, and 3.410, respectively (P < 0.05 for all). On the other hand, HDL-C was negatively correlated with the risk of AMI, with an OR value of 0.034 (P < 0.001). However, there were no significant differences between the AMI and control groups in terms of TG, alcohol consumption, and LDL-C concerning the AMI risk (P > 0.05 for each).

4.4. Frequencies of SNP rs17465637 and Clinical Characteristics

As shown in Table 4 The frequency of the CC genotype of SNP rs17465637 SNPs was the highest (kappa = -0.011, P < 0.05). No significant differences were seen in allelic frequencies of rs17465637 between the control subjects and the AMI patients (kappa = -0.078, P > 0.05). There were no significant differences in genotype and allele frequencies of SNP rs17465637 between the other three subgroups (diagnosis time, typical symptoms, and serious complications) (P > 0.05 for all) (Tables 5-7).

4.5. Interactions Between SNP rs17465637 and BMI, Smoking, and Alcohol Consumption

In Table 8, there were significant interactions between the presence of the CC genotype and BMI or smoking (P < 0.007 for both). Subjects carrying the CC genotype with BMI ≥ 24 kg/m^2 had an increased risk of AMI as 406.0% (P < 0.007). The subjects who smoked ≥ 20 cigarettes/day carrying the CC genotype had an increased risk of AMI (OR = 2.732, P < 0.007). No interactions were seen between the CC and CA genotypes and BMI, smoking, or alcohol consumption (P > 0.007 for all).

5. Discussion

Genome-wide association studies (GWAS) have been very successful in identifying genetic variations to determine risk factors and individual differences in coronary events (20, 28). Many cardiovascular risk factors and biomarkers are linked and dozens of alleles are considered to be at the root of many common diseases or characteristics (29). The MIA SH3 Domain ER Export Factor 3 (MIA3) gene encoding the 14 kDa protein of unknown function was originally identified as a new member of the MIA gene family (30). MIA3 is largely expressed in relation to the very restricted expression patterns of other family members (31, 32). At present, there is scarce information on the interaction between SNP rs17465637 and AMI in Chinese Han populations. In this study, the AA genotype of SNP rs17465637 was positively correlated with the risk of AMI. In a previous study, the risk of SNP rs17465637 in MIA3 was associated with coronary artery disease by increasing the rates of TG and was supported by the Pakistani population and Caucasians (33, 34). Recent GWAS have revealed an association between the MIA3 gene and LDL-C levels and the risk of AMI (13, 35). Some studies observed that MIA3

Table 1. General Characteristics and Serum Lipid Levels in AMI and Control Groups

Parameter	AMI Group	Control Group	$t(\chi^2)$ z	P Value
Number	344	344	-	-
Male/female	266/78	238/106	-2.410	0.016
Age, y	61.61 ± 10.73	57.86 ± 10.86	4.558	< 0.001
Body mass index, kg/m²	23.76 ± 3.47	22.49 ± 3.14	5.078	< 0.001
Cigarette smoking, No. (%)	-	-	63.155	< 0.001
Nonsmoker	170 (49.40)	261 (75.87)	-	-
≤ 20 cigarettes/day	44 (12.80)	40 (11.63)	-	-
> 20 cigarettes/day	130 (37.80)	43 (12.50)	-	-
Alcohol consumption, No. (%)	-	-	59.932	< 0.001
Nondrinker	260 (75.60)	280 (81.40)	-	-
≤ 25 g/day	32 (9.30)	63 (18.31)	-	-
> 25 g/day	52 (15.10)	1 (0.29)	-	-
Total cholesterol, mmol/L	4.56 ± 1.25	4.25 ± 0.89	-3.731	< 0.001
Triglycerides, mmol/L	1.64 ± 1.09	1.40 ± 1.05	0.358	0.003
LDL-C, mmol/L	2.72 ± 0.99	2.84 ± 0.84	-1.691	0.091
HDL-C, mmol/L	1.13 ± 0.33	1.70 ± 0.40	-20.717	< 0.001

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

Table 2. Distribution Difference in rs17465637 Genotype and Allele Frequency Between AMI and Control Groups

Parameter	AMI Group, No. (%)	Control Group, No. (%)	Kappa	χ^2	P Value
Number (n = 688)	344 (50.00)	344 (50.00)	-	-	-
Genotypes	-	-	-0.082	16.909	< 0.001
CC	146 (42.44)	135 (39.24)	-	-	-
CA	119 (34.5)	164 (47.67)	-	-	-
AA	79 (22.97)	45 (13.08)	-	-	-
Allele	-	-	-0.033	1.622	0.203
C	411 (59.73)	434 (63.08)	-	-	-
A	277 (40.27)	254 (36.92)	-	-	-

may be involved in promoting the migration of monocytes through fibrinogen or Human Microvascular Endothelial Cells (HMEC) (17, 34). In addition, the expression of MIA3 was induced after human monocyte adhesion to the substrate and it was found that the recombinant MIA3 protein reduced human monocyte attachment to fibrinogen, intercellular adhesion molecule-1 (ICAM-1), and HMEC (36). These results indicate that MIA3 reduces adhesion to fibrinogen or other cell adhesion molecules. This process is essential for the formation and development of atherosclerotic plaques and their instability, which could play a significant role in the development of coronary atherosclerosis (37). For the first time, our study showed that the AA genotype of SNP rs17465637 was positively correlated with extensive anterior of AMI. The relevant underlying mechanism is unknown. It is inferred that the MIA3 gene can affect the stability of atherosclerotic plaques or the growth of human vascular smooth muscle in AMI. In addition, we found that the interaction between the CC genotype of SNP rs17465637 and BMI or smoking appeared to increase the risk of AMI. It was also confirmed that diabetes, high blood pressure, BMI, sex, TC, age, and smoking were the risk factors of AMI, while HDL-C was negatively correlated with the AMI risk, similar to our previous study (33). AMI is a multifactorial disease characterized by complex pathogenesis involving unique genetic inheritance, lifestyle, and environmental risk factors (38). A great deal of evidence has confirmed that the risk factors for AMI include dia-

Table 3. The Risk Factor Analysis of AMI

Parameter	B	SE	Wald	Sig.	Exp(B)/OR
Diabetes	4.235	1.054	16.153	< 0.001	69.087
rs17465637	0.342	0.150	5.232	0.022	1.408
High blood pressure	2.737	0.286	91.566	< 0.001	15.436
Age	0.645	0.245	6.940	0.008	1.906
Smoking	1.227	0.150	66.570	< 0.001	3.410
HDL-C	-3.395	0.584	33.796	< 0.001	0.034
Sex	0.720	0.286	6.358	0.012	2.055
BMI	0.550	0.188	8.536	0.003	1.733
TC	0.935	0.443	4.463	0.035	2.547
TG	0.105	0.260	0.163	0.687	1.110
Alcohol consumption	-0.005	0.098	0.003	0.960	0.995
LDL-C	0.229	0.411	0.312	0.577	1.258

Abbreviations: HDL-C; high-density lipoprotein cholesterol; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides

Table 4. Comparison of Genotype and Allele Between Different Infarct Sites

Parameter	Groups, No. (%)						Kappa	χ^2	P Value
	Extensive Anterior	Inferior	Anteroseptal	Lateral	Right Ventricular	Multivessel Lesion			
Number (n = 344)	182 (52.91)	118 (34.30)	23 (6.68)	7 (2.03)	13 (3.78)	1 (0.30)	-		-
Genotype	-	-	-	-	-	-	-0.011	20.50	0.025
CC	68 (37.36)	50 (42.37)	13 (56.52)	4 (57.14)	10 (76.92)	1 (100.0)	-	-	-
CA	60 (32.97)	49 (41.53)	6 (26.09)	1 (14.29)	3 (23.08)	0 (0.00)	-	-	-
AA	54 (29.67)	19 (16.10)	4 (17.39)	2 (28.57)	0 (0.00)	0 (0.00)	-	-	-
Allele	-	-	-	-	-	-	-0.078	3.250	0.662
C	196 (53.80)	149 (63.10)	32 (69.57)	9 (64.28)	23 (88.46)	2 (100.0)	-	-	-
A	168 (46.20)	87 (36.86)	14 (30.43)	5 (35.71)	3 (11.54)	0 (0.00)	-	-	-

Table 5. The Comparison of Genotype and Allele of rs17465637 Between Different Diagnosis Times

Parameter	Groups, No. (%)				Kappa	χ^2	P Value
	DT $\leq$ 2 h	2 h< DT $\leq$ 6 h	6 h < DT $\leq$ 12 h	DT > 12 h			
Number (n = 344)	58 (16.86)	121 (35.17)	114 (33.14)	51 (14.83)	-	-	-
Genotype	-	-	-	-	0.017	1.369	0.968
CC	25 (43.10)	50 (41.32)	47 (41.23)	24 (47.06)	-	-	-
CA	20 (34.48)	43 (35.54)	38 (33.33)	18 (35.29)	-	-	-
AA	13 (22.41)	28 (23.14)	29 (25.44)	9 (17.65)	-	-	-
Allele	-	-	-	-	0.005	1.468	0.690
C	69 (60.53)	143 (59.09)	133 (57.83)	66 (64.71)	-	-	-
A	45 (39.47)	99 (40.91)	97 (42.17)	36 (35.29)	-	-	-

Abbreviations: DT, diagnosis time (time until diagnosis)

betes, high blood pressure, poor diet, high blood cholesterol, obesity, smoking, lack of exercise, and excessive alcohol intake (33, 39). SNP rs17465637 in MIA3 demonstrated significant genotype associations with MI. While lifestyle is a key risk factor, much of the international variation is due to genetic factors (40). Thus, it is vital to understand the genomic milieu of individuals developing AMI, which may help in identifying individual susceptibility to AMI.

Some studies have shown that telomere shortening is associated with the pathogenesis of atherosclerosis and

Table 6. Comparison of Genotype and Allele Between Severe Complications Group and Non-Severe Complications Group

Parameter	Groups, No. (%)		Kappa	χ^2	P Value
	Complications (2 h < DT ≤ 6 h)	Non-Complications (DT > 12 h)			
Number (n = 344)	294 (85.47)	50 (14.53)	-	-	-
Genotype	-	-	-0.034	3.672	0.159
CC	128 (43.54)	38 (54.29)	-	-	-
CA	97 (32.99)	22 (31.43)	-	-	-
AA	69 (23.47)	10 (14.29)	-	-	-
Allele	-	-	0.001	0.147	0.701
C	353 (60.03)	58 (58.00)	-	-	-
A	235 (39.97)	42 (42.00)	-	-	-

Table 7. Comparison of Genotype and Allele Between Typical Symptom Group and Non-Typical Symptom Group

Parameter	Groups, No. (%)		Kappa	χ^2	P Value
	Typical Symptom (2 h < DT ≤ 6 h)	Non-Typical Symptom (DT > 12 h)			
Number (n = 344)	86 (25.00)	258 (75.00)	-	-	-
Genotype	-	-	-0.011	0.145	0.930
CC	108 (41.86)	38 (44.19)	-	-	-
CA	90 (34.88)	29 (33.72)	-	-	-
AA	60 (23.26)	19 (22.09)	-	-	-
Allele	-	-	-0.014	0.163	0.686
C	306 (59.30)	105 (61.05)	-	-	-
A	210 (40.70)	67 (38.95)	-	-	-

acute vascular syndrome and some studies have indicated that short telomere length increases the risk of MI (35). Besides, it has been verified that lifestyle is one of the strongest predictors of CAD risk and that this increased risk may stem from effects on the telomere length (41). For example, a sedentary lifestyle may accelerate the aging process (42). Various cardiovascular risk factors such as obesity, smoking, and sex may be related to the regulation of the sample length (43). Some studies have shown that smoking can be linked to normal telomeres and thin, obese women (44). Another study demonstrated that men with lower vitamin C intake were most likely to suffer from AMI. In addition, the shortening of telomeres has been correlated with hypertensive and diabetic patients (45). Several environmental factors have been documented to influence biological mechanisms but little is known about gene-environment interaction effects. Therefore, further studies are required to elucidate the underlying cause of associations identified in this study.

5.1. Conclusions

In conclusion, data from this study indicate that the mutant AA genotype of SNP rs17465637 in MIA3 was positively associated with the AMI risk. Also, the interaction between the CC genotype of SNP rs17465637 and BMI and smoking appeared to increase the risk of AMI. In addition, we discovered that the AA genotype of SNP rs17465637 was positively correlated with extensive anterior of AMI. Finally, it was confirmed that diabetes, high blood pressure, BMI, sex, TC, age, and smoking were the risk factors of AMI, while HDL-C was negatively correlated with the AMI risk.

Our research had several potential limitations. First, the sample in the study was small, which might limit some potential for discovery. Second, the association between the AA genotype of SNP rs17465637 and the extensive anterior of AMI suffered from sufficient objectivity and supporting material. Third, race differences could also have led to biased results. In addition, SNPs-SNPs interactions associated with AMI were not considered in our study.

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Table 8. Interaction Between Genotypes of rs17465637 and Environmental Factors in the Impact of AMI

Genotypes	Environmental Factor	B	SE	Wald	Sig.	Exp (B)/OR	95% CI for OR	
							Lower	Upper
-	**BMI (kg/m^2)**	-	-	-	-	-	-	-
CC	0 - 19	-	-	15.649	< 0.001	-	-	-
CC	19 - 24	0.531	0.439	1.459	0.227	1.700	0.719	4.020
CC	≥ 24	1.401	0.450	9.684	0.002	4.060	1.680	9.812
CA+AA	0 - 19			0.138	0.933			
CA+AA	19 - 24	-0.038	0.586	0.004	0.948	0.963	0.305	3.037
CA+AA	≥ 24	-0.153	0.603	0.064	0.800	0.858	0.263	2.798
-	**Smoking (n/d)**	-	-	-	-	-	-	-
CC	0	-	-	11.196	0.004	-	-	-
CC	0 - 20	0.004	0.348	0.000	0.991	1.004	0.507	1.987
CC	≥ 20	1.005	0.307	10.685	0.001	2.732	1.495	4.991
CA+AA	0	-	-	7.257	0.027	-	-	-
CA+AA	0 - 20	0.949	0.484	3.847	0.050	20582	1.001	6.664
CA+AA	≥ 20	0.903	0.409	4.874	0.027	2.466	1.107	5.495
-	**Alcohol (g/d)**	-	-	-	-	-	-	-
CC	0	-	-	6.951	0.073	-	-	-
CC	0 - 250	-0.944	0.358	6.951	0.008	0.389	0.193	0.785
CC	≥ 250	21.095	10048.243	0.000	0.998	1.450E9	0.000	-
CA+AA	0	-	-	1.608	0.448	-	-	-
CA+AA	0 - 250	0.600	0.473	1.608	0.205	1.822	0.721	4.607
CA+AA	≥ 250	0.316	12076.485	0.000	1.000	1.371	0.000	-

Abbreviations: BMI, body mass index; g/d, grams of alcohol consumed per day, n/d, number of cigarettes smoked per day.

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Footnotes

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