Correlation of rs1122608 SNP with acute myocardial infarction susceptibility and clinical characteristics in a Chinese Han population: A case-control study

Quan-fang Chen, Wei Wang, Zhou Huang*, Dong-ling Huang*, Tian Li*, Fan Wang*, Jun Li**

Department of Institute of Respiratory Disease and, *Department of Emergency, The First Affiliated Hospital, Guangxi Medical University; Guangxi-*People's Republic of China*

Abstract

Objective: The correlation of the *BRG1* rs1122608 single nucleotide polymorphism (SNP) with acute myocardial infarction (AMI) has been reported in American and European populations. However, whether rs1122608 acts as a protective factor or a risk factor for AMI is controversial. In this study, we aimed to detect the associations between rs1122608 and the clinical characteristics of AMI as well as susceptibility, gene–environment interactions, and risk factors for AMI in a Chinese Han population.

Methods: In this study, 300 AMI patients and 300 healthy controls of Chinese Han ancestry were enrolled. PCR-RFLP was used to genotype rs1122608 SNPs. Genotypic and allelic frequencies of rs1122608 were compared between the AMI and control groups and among four AMI subgroups, which were subdivided by typical symptom, diagnosis time (DT), infarction location andserious complication.

Results: Significant differences were detected between the AMI patients and the controls in both the genotypic and allelic frequencies of rs1122608 ($p<0.001$ for each). There were also interactions between the subjects with a minor T allele and smoking or alcohol consumption ($p<0.001$ for each).

Conclusion: In the Chinese Han study population, the mutant GT and TT genotypes and minor T allele of rs1122608 were positively correlated with the risk of AMI. For the first time, we discovered that the GT genotype of the rs1122608 SNP is significantly correlated with diagnosis time of AMI. In addition, the interactions between the minor T allele of rs1122608 and smoking or alcohol use and between the rs1122608 CC genotype and alcohol use appear to increase the risk of AMI. *(Anatol J Cardiol 2018; 19: 249-58)*

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

Introduction

Acute myocardial infarction (AMI) occurs when atherosclerotic coronary artery plaque erosion or rupture causes complete, partial, and/or transient 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 USA, AMI occurs in approximately 1.5 million residents 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 others (2, 3). In China, >8 million people suffer from AMI, and up to 23 million people are predicted to suffer from AMI in 2030 (4). AMI has become one of the most dangerous disorders in humans, resulting in a heavy medical and financial burden, with serious effects on the quality of life of the citizens. AMI is a complex clinical phenomenon that involves multiple factors, both environmental and genetic, and their interactions (5). In 2009, 10 loci associated with AMI, including the rs1122608 single nucleotide polymorphism (SNP), were identified by the Myocardial Infarction Genetics Consortium (6). One report of Iranian populations showed that homozygote genotypes for the rs1122608 SNP have a strong protective effect against CAD (7). However, the role of rs1122608 remains controversial; it is unclear whether this SNP acts as a protective factor or as a risk factor for AMI. Furthermore, the association between rs1122608 and the clinical characteristics of AMI, such as early diagnosis, infarct location, and ventricular fibrillation, has not been reported previously. Here, we assess whether rs1122608 SNP and its interaction with environmental factors is related to susceptibility to, risk factors for, and clinical characteristics of AMI in people of Chinese Han ancestry.

Address for correspondence: Wei Wang, MD, Department of Emergency, The First Affiliated Hospital, Guangxi Medical University, 6 Shuangyong Road Nanningh, Guangxi-*People's Republic of China*
Phone: +86-13507715528 E-mail: weiwanggx@163.com

Accepted Date: 19.02.2018 **Available Online Date:** 29.03.2018

DOI:10.14744/AnatolJCardiol.2018.35002

Anatol J Cardiol 2018; 19: 249-58
DOI:10.14744/AnatolJCardiol.2018.35002

Methods

Study population

In total, 300 AMI patients who had been diagnosed in the Emergency Department of Guangxi Medical University, Guangxi province, People's Republic of China (8), and 300 healthy control subjects who were matched for age, lifestyle, and socioeconomic status, all from Guangxi province, were enrolled in the present study from January 1, 2012, to December 31, 2014. The AMI patient group comprised 228 (76.0%) males and 72 (24.0%) females ranging from 33 to 84 years of age. The mean age of the AMI patients was 61.67±10.43 years. The healthy control subjects comprised 210 (70.0%) males and 90 (30.0%) females, aged 34 to 83 years. The mean age of the control subjects was 58.49±10.54 years. The present study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. All subjects received a full explanation of the study, and after receiving this explanation, they provided informed consent.

Subgroups

To assess the relationship between rs1122608 and clinical characteristics, the 300 cases comprising the AMI group were subdivided as follows. 1) They were subdivided into two subgroups: 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 subdivided into two subgroups according to whether or not serious complications developed: no serious complications (n=275) and serious complications (n=25).

Epidemiological survey

Standardized questionnaires were used to collect information on lifestyle factors, socioeconomic status, and other demographic aspects of the study subjects. Information on ethanol consumption included questions about the number of liangs (about 50 g) of beer, corn wine, rice wine, rum, or other liquor consumed over the course of the previous year. Ethanol consumption was categorized into two groups, ≤ 250 g and > 250 g, according to the grams of ethanol consumed daily. Smoking status was categorized into two groups on the basis of the number of cigarettes, ≤20 and >20, smoked per day. Under the supervision of two observers, weight, waist circumference, and height were measured. Each reported blood pressure value is the average of three separate measurements, with each measurement separated from the previous measurement by a 15-min rest period. Assessment of blood pressure was performed in seated patients using a mercury sphygmomanometer. To calculate body mass index (BMI), weight in kg was divided by height in meters squared (kg/m^2).

Biochemical analysis

Biochemical assessments were performed using internationally standardized methods (9). Serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), cardiac troponin I (cTnI), and creatine kinase-MB (CK-MB) levels were obtained from samples analyzed by the biochemical laboratory of the First Affiliated Hospital of Guangxi Medical University.

DNA extraction, amplification, and genotyping

The phenol-chloroform method was used for the extraction of genomic DNA from peripheral blood leukocytes (10), and this gDNA was stored at 4°C for future analysis. The primers used to genotype the rs1122608 SNP were the sense primer 5′-GAACGCCCCTCAAGCTGCCCTCC-3′ and the anti-sense primer 5′-AGCCACCGTGCCCAGCC-TCCAA-3′ (Sangon, Shanghai, PRC). PCR reaction volumes were 20 μL and were composed of 1.0 μL of gDNA, 10 μL of 2×Taq PCR Mastermix (0.1 U Taq polymerase/μL, 500 μM of each dNTP, 20 mM Tris-HCl, pH 8.3, 100 mM KCl, 3 mM $MgCl_2$), 0.8 μL of each primer (10 pmol/L), and 8 μL of ddH_2O (DNase/RNase-free). The thermocycling conditions for the PCR were as follows: denaturation at 95°C for 5 min, then 35 cycles of 95°C for 30 s, 63°C for 30 s, and 72°C for 30 s. Following these 35 cycles, an extension step at 72°C was performed for 7 min. The PCR products were then digested at 37°C overnight in a volume of 5 mL using 5 U of *BsrI* (New England Biolabs, Inc, Beverly, MA, USA). To identify the genotypes, after restriction digestion of the amplified gDNA, the fragments were separated by electrophoresis on 2% agarose gels containing ethidium bromide and were visualized under ultraviolet illumination. Scoring of genotypes was performed by an experienced reader who was blinded to the serum lipid levels and epidemiological data. Direct sequencing was used to confirm six of the samples (genotypes: 2 GG, 2 TT, and 2 GT) that had been assessed as positive according to PCR-RFLP. Low melting point gel electrophoresis and phenol extraction to purify the PCR products were followed by analysis of the DNA sequences by Shanghai Sangon Biological Engineering Technology & Services Co., Ltd., PRC.

Diagnostic criteria

The guidelines of the European Resuscitation Council formed the basis of the diagnostic criteria and study protocol (8, 11, 12). A diagnosis of ST-segment elevation myocardial infarction (STEMI) was mandatory for inclusion in the present study. STEMI was defined as follows: ST-segment elevation of 1 mm or greater in at least two contiguous leads of a 12-lead electrocardiogram; cardiac biomarkers and troponin and/or CK-MB elevated to over twice the upper limit of normal laboratory reference values; prolonged chest discomfort typical of myocardial ischemia; and confirmation by coronary artery radiography. Ventricular fibrillation was defined according to the following atypical electrocardiogram patterns: heart rate between 150 and 500 beats/min; chaotic and/or irregular deflections of varying amplitude; and

Table 1. General characteristics and serum lipid levels between the acute myocardial infarction 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

AMI - acute myocardial infarction; HDL-C - high-density lipoprotein cholesterol; LDL-C - low-density lipoprotein cholesterol

no identifiable P waves, QRS complexes, or T waves. Shock was defined according to the following criteria: confusion; pale and clammy skin; high heart rate (>120 beats/min); and systolic blood pressure <90 mm Hg. Heart failure diagnosis was determined on the basis of brain natriuretic peptide and heart ultrasound. Serum levels of TG, TC, LDL-C, HDL-C, cTnI, and CK-MB were measured at our Clinical Science Experiment Center. The values for normal serum TG, TC, LDL-C, HDL-C, cTnI, and CK-MB were designated as 0.56-1.70 mmol/L, 3.10-5.17 mmol/L, 2.70-3.20 mmol/L, 0.91-1.81 mmol/L, 0-0.014 ng/mL, and 0-25 μg/L, respectively. The 2003 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension (13) were used as the criteria for the diagnosis of hypertension. Obesity, overweight, and normal weight were defined as BMI values of >28, 25-28, or 19-24 kg/m^2, respectively (14).

Statistical analyses

Quantitative variables were presented as mean±SD Qualitative variables were presented as raw count and percentage. Genotypic and allelic frequencies were assessed by direct counting. Pearson's X^2 test was used to evaluate between-group differences in sex ratio and genotype distribution. A Student's unpaired t-test was used to evaluate difference in general characteristics between the AMI and control groups. 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. P<0.05 (two-tailed) was considered statistically significant. When we estimated the interactions between the rs1122608 SNP and BMI, ethanol consumption, and cigarette smoking, a value of p<0.017 (corresponding to a value of p<0.05 after adjustment via Bonferroni correction for three independent tests) was considered statistically significant. Odds ratios (ORs) were also calculated along with their corresponding 95% confidence intervals (95% CI). The statistical software package SPSS 20.0 (SPSS Inc., Chicago, Illinois, USA) was used to perform all statistical analyses.

Results

Subjects' general characteristics and serum lipid levels

Comparison of generalized features is present 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) values were higher in the AMI patients than in the control subjects. The numbers (percentages) of AMI patients who consumed alcohol and smoked were 74 (24.67%) and 144 (48.00%), respectively, and the numbers (percentages) of control subjects who consumed alcohol and smoked were 60 (20.00%) and 75 (25.00%), respectively. Significantly more subjects in the AMI group smoked and consumed alcohol compared with the non-AMI controls (p<0.001 for each). There were no significant differences in sex ratio between the AMI patients and the controls (p>0.05).

Comparison of the lipid levels is also shown in Table 1. TC, TG, and LDL-C levels were 5.20±0.95 mmol/L, 1.66±1.13 mmol/L, and

Anatol J Cardiol 2018; 19: 249-58
DOI:10.14744/AnatolJCardiol.2018.35002

Table 2. Distribution difference of rs1122608 genotype and allele frequency between the acute myocardial infarction and control groups

Parameter	AMI group [n (%)]	Control group [n (%)]	X^2	*P*
Number (n=600)	300 (50.00)	300 (50.00)	-	-
Genotypes	-	-	213.22	< 0.001
GG	71 (23.67)	248 (82.67)	-	-
GT	150 (50.00)	43 (14.33)	-	-
TT	79 (26.33)	9 (3.00)	-	-
Allele	-	-	23.882	< 0.001
G	292 (48.67)	539 (89.83)	-	-
T	308 (51.33)	61 (10.17)	-	-

AMI - acute myocardial infarction

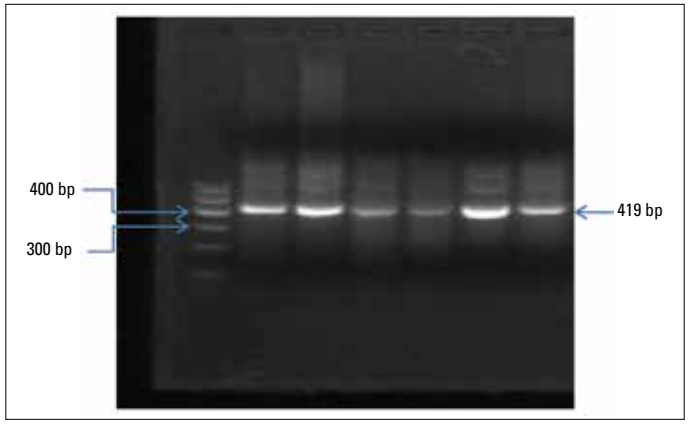

Figure 1. Gel electrophoresis of rs1122608 PCR amplification products in *BRG1*

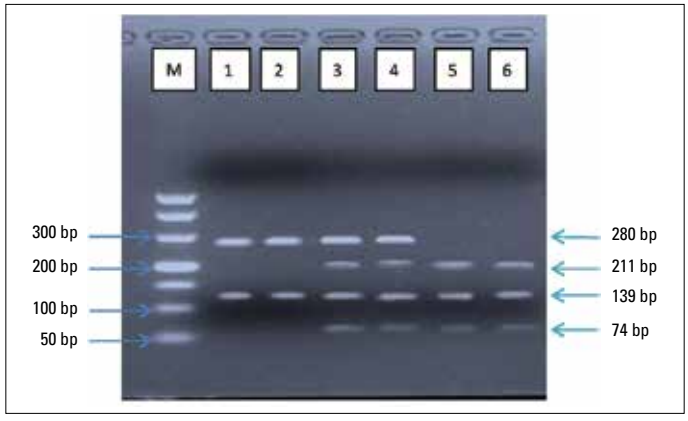

Figure 2. Genotyping of rs1122608 polymorphism within *BRG1*

3.71±0.92 mmol/L in the AMI group, respectively, and 4.97±1.05 mmol/L, 1.45±1.11 mmol/L, and 2.89±0.87 mmol/L in the control group, respectively. Serum TC, TG, and LDL-C levels in the AMI group were higher than those in the control group (p<0.05 for each). The serum HDL-C levels in the AMI group were lower than those in the control group (1.08±0.26 mmol/L vs. 1.36±0.25 mmol/L, p<0.001).

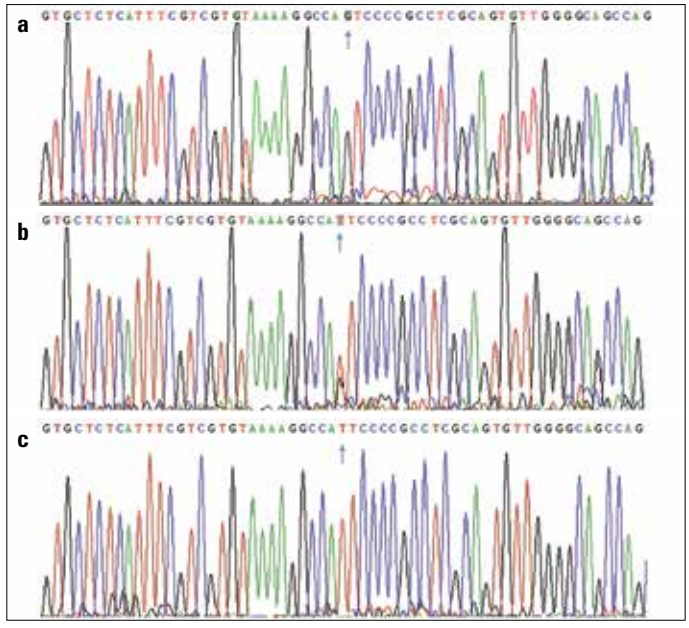

Figure 3. Partial nucleotide sequence of rs1122608 in *BRG1*

Electrophoresis, sequencing, and genotyping

Amplification of gDNA yielded PCR products of 419 bp (Fig. 1). The identified genotypes were named according to the presence (G allele) or absence (T allele) of the restriction sites, with the GG genotype designated as the wild-type homozygote. This wild-type GG genotype was characterized by the absence of the restriction site (with bands at 280 and 139 bp; lanes 1 and 2; Fig. 2). The heterozygotic GT genotype included both the absence and presence of the restriction site (with bands at 280, 139, 211, and 74 bp; lanes 3 and 4; Fig. 2). The homozygotic CC genotype included only the presence of the mutated site (bands at 139, 211, and 74 bp; lanes 5 and 6; Fig. 2). Sequencing was performed to confirm the GG, GT, and TT genotypes initially identified by the PCR-RFLP (Fig. 3).

Genotypic and allelic frequencies

The frequencies of rs1122608 SNPs, both genotypic and allelic, are shown in Table 2. The wild-type GG genotype and G

Table 3. Risk factor analysis of acute myocardial infarction

Parameter	B	SE	Wald	Sig	Exp(B)/OR
Diabetes	4.237	1.155	13.461	<0.001	69.214
rs1122608	2.775	0.304	83.204	<0.001	16.038
High blood pressure	2.206	0.362	37.086	<0.001	9.080
Age	1.563	0.327	22.828	<0.001	4.775
Smoking	1.542	0.250	38.038	<0.001	4.674
HDL-C	-2.953	0.724	16.639	<0.001	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
Alcohol consumption	0.192	0.258	0.554	0.457	1.313
LDL-C	0.184	0.553	0.110	0.740	1.202

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

Table 4.1. Comparison of genotypes and alleles of rs1122608 among different diagnosis times

Parameter	Groups [n (%)]				X^2	*P*
	DT≤2h	2h<DT≤6h	6h<DT≤12h	DT>12h		
Number (n=300)	40 (13.33)	119 (39.67)	116 (38.67)	25 (8.33)	-	
Genotype	-	-	-	-	4.875	0.560
GG	5 (12.50)	29 (24.37)	31 (26.72)	6 (24.00)	-	
GT	21 (52.50)	62 (52.10)	56 (48.28)	11(44.00)	-	
TT	14 (35.00)	28 (23.53)	29 (25.00)	8 (32.00)	-	
Allele	-	-	-	-	4.032	0.258
G	31 (38.75)	120 (50.42)	118 (50.86)	23 (46.00)	-	
T	49 (61.25)	118 (49.58)	114 (49.14)	27 (54.00)	-	

Table 4.2. Comparison of genotypes and alleles between the severe complications group and non-severe complications group

Parameter	Groups [n (%)]		X^2	*P*
	Complications	Non-complications		
Number (n=300)	275 (91.67)	25 (8.3)	-	-
Genotype	-	-	0.654	0.721
GG	64 (23.27)	7 (28.00)	-	-
GT	137 (49.82)	13 (52.00)	-	-
TT	74 (26.91)	5 (20.00)	-	-
Allele	-	-	0.621	0.431
G	265 (48.18)	27 (54.00)	-	-
T	285 (51.82)	23 (46.00)	-	-

allele frequencies, respectively, were 23.67% and 48.67% in the AMI patients. These frequencies were significantly lower than those in the control subjects, 82.67% and 89.83%, respectively. The frequencies of the GT and TT genotypes and of the minor

Anatol J Cardiol 2018; 19: 249-58
DOI:10.14744/AnatolJCardiol.2018.35002

Table 4.3. Comparison of genotypes and alleles between the typical symptom group and non-typical symptom group

Parameter	Groups [n (%)]		X^2	*P*
	Typical symptom	Non-typical symptom		
Number (n=300)	78 (26.00)	222 (74.00)	-	-
Genotype	-	-	2.082	0.353
GG	23 (29.49)	48 (21.62)	-	-
GT	35 (44.87)	115 (51.80)	-	-
TT	20 (25.64)	59 (26.58)	-	-
Allele	-	-	0.895	0.344
G	81 (51.92)	211 (47.52)	-	-
T	75 (48.08)	233 (52.48)	-	-

Table 4.4. Comparison of genotypes and alleles 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	-	-	-	-	-	-	5.841	0.828
GG	30 (21.28)	24 (24.75)	6 (33.33)	2 (28.57)	4 (30.77)	5 (20.83)	-	
GT	76 (53.90)	47 (48.45)	9 (50.00)	3 (42.86)	6 (46.15)	9 (37.50)	-	
TT	35 (24.82)	26 (26.80)	3 (16.67)	2 (28.57)	3(23.07)	10 (41.67)	-	
Allele	-	-	-	-	-	-	3.250	0.662
G	136 (48.23)	95 (48.97)	21 (58.33)	7 (50.00)	14 (53.85)	19 (39.58)	-	
T	146 (51.77)	99 (51.03)	15 (41.67)	7 (50.00)	12 (46.15)	29 (60.42)	-	

T allele were 50.00%, 26.33%, and 51.33%, respectively, in the AMI group. These frequencies were significantly higher than the 14.33%, 3.00%, and 10.17% seen in the control group. Significant differences in both the genotypic and allelic frequencies were detected between the AMI and control groups ($p<0.001$ for each).

Risk factors for AMI

Non-conditional binary logistic regression analysis showed that diabetes, rs1122608, high blood pressure, age, smoking, and sex were strongly associated with the risk of AMI, with OR values of 69.214, 16.038, 9.080, 4.775, 4.674, and 2.235, respectively (Table 3). In contrast, HDL-C was negatively correlated with the risk of AMI, with an OR value of 0.052 ($p<0.05$ for each). However, no significant differences were observed between the AMI patients and the control subjects in terms of correlation of BMI, TC, TG, alcohol consumption, and LDL-C with the risk of AMI ($p>0.05$ for each).

Frequencies of rs1122608 and clinical characteristics

No significant differences were seen in the genotypic and allelic frequencies of rs1122608 between the control subjects and the AMI patients, including AMI subgroups divided according to DT, typical symptoms, serious complications, and infarction location ($p>0.05$ for each) (Table 4-1–4-4).

Interactions between rs1122608 and BMI, smoking, or alcohol consumption

As showed in Table 5, there were significant interactions between presence of the minor T allele and smoking or alcohol consumption ($p<0.001$ for each). The subjects carrying the minor T allele differed in terms of increased risk of AMI, with light smokers (<20 cigarettes/day) having an increased risk of AMI of 899.4% and heavy smokers (≥20 cigarettes/day) having an increased risk of AMI of 588.5%. The subjects who consumed <250 g/day or ≥250 g/day of alcohol and who also had the minor T allele were at a 1,166.7% or 3,000% increased risk of AMI, respectively. There was no significant interaction between presence of the minor T allele and BMI ($p>0.007$). The subjects who consumed <250 g/day of alcohol and who had the GG genotype were at a 24,545% increased risk of AMI ($p<0.017$). No interactions were seen among the GG genotype and BMI or smoking that affected the risk of AMI ($p>0.017$ for each).

Table 5. Interaction between the genotypes of rs1122608 and environment factors on the impact of acute myocardial infarction

Genotypes	Environment factor	B	SE	Wald	Sig	Exp (B)/OR	95.0% CI for OR	
							Lower	Upper
-	**BMI (Kg/m²)**	-	-	-	-	-	-	
GG	19-24	-	-	74.783	<0.001	-	-	
GG	≥24	0.585	0.300	3.793	0.051	0.051	0.996	3.231
GT+TT	19-24	-	-	52.805	<0.001	-	-	
GT+TT	≥24	0.653	0.316	4.276	0.039	1.921	1.053	3.568
-	**Smoking (n/d)**	-	-	-	-	-	-	
GG	0	-	-	0.262	0.877	-	-	
GG	0-20	20.485	4.947 E4	0.000	0.997	7.884E8	-	
GG	≥20	20.327	4.947 E4	0.000	0.997	6.731 E8	-	
GT+TT	0	-	-	24.468	< 0.001	-	-	
GT+TT	0-20	2.197	0.444	24.468	< 0.001	8.994	3.767	21.474
GT+TT	≥20	1.772	0.508	12.177	< 0.001	5.885	2.175	15.924
-	**Alcohol (g/d)**	-	-	-	-	-	-	
GG	0	-	-	9.859	0.007	-	-	
GG	0-250	2.559	1.024	20.974	0.012	12.928	1.737	96.209
GG	≥250	3.201	1.068	6.246	0.003	24.545	3.028	198.960
GT+TT	0	-	-	20.985	< 0.001	-	-	
GT+TT	0-250	2.457	0.201	16.706	< 0.001	11.667	3.592	37.894
GT+TT	≥250	3.401	0.780	19.016	< 0.001	30.000	6.505	138.364

Discussion

Genome-wide association studies have identified rs1122608 SNP, located in intron 30 of SMARCA4 (aka *BRG1*), as a risk variant for AMI and CAD (6). Initially, rs1122608 was thought to be located in LDLR and to affect the onset of AMI by regulating LDL-C levels. However, more recently, *BRG1/SMARCA4* has been confirmed as the location of this SNP, approximately 36 kb from LDLR. Moreover, much evidence has verified that rs1122608 is related to CAD independently of lipid profiles (15, 16).

In the present study, we show that the mutant GT and TT genotypes and the minor T allele of the *BRG1* rs1122608 SNP were positively correlated with AMI morbidity. At present, there is little information on the interaction between rs1122608 and AMI in Chinese populations. The mechanisms underlying the involvement of *BRG1* in the elevated risk of AMI are still unclear. Mutations in *BRG1/SMARCA4* were initially recognized in human lung cancer cell lines (17). Located on chromosome 19p13.2 and containing 36 exons, *BRG1/SMARCA4* encodes the catalytic subunit of the large, ATP-dependent SWI/SNF chromatin remodeling complex. This complex, which is required for the transcriptional activation of genes normally repressed by chromatin, influences transcriptional regulation in an ATP-dependent manner by the disruption of histone-DNA contacts. The protein encoded by *BRG1* is similar to the Brahma protein of *Drosophila*. As a member of the SWI/SNF family of proteins, which are characterized by helicase and ATPase activities, the SWI/SNF proteins can be expected to have roles in the regulation of transcription of certain genes by altering the structure of the surrounding chromatin. Much evidence has indicated that *BRG1* can affect the occurrence of AMI through the regulation of vascular smooth muscle. Some knockout research has indicated that *BRG1* aids in smooth muscle development. *BRG1* knockouts lack contractility in their gastrointestinal smooth muscle, and intestines are even incomplete in some cases. Importantly, another defect that occurs in *BRG1* knockouts is heart complications, for example, open ductus arteriosus after birth (18, 19). Previous research has shown that microRNAs play key roles in smooth muscle cell (SMC) development and maintenance in both gastrointestinal and vascular tissues. The most abundant Dicer-dependent microRNAs in SMCs are miR-143 and miR-145. These two miRs are encoded by a bicistronic primary microRNA transcript that is later processed into two separate mature microRNAs (20). Although miR-143/145 knockout mice are viable, they are characterized by substantially reduced blood pressure, thinner vascular smooth muscle layers, incomplete differentiation of SMCs, and altered formation of the neointima in response to vascular injury (21, 22). MiR-133, a microRNA that has been thought of as specific to cardiac and skeletal muscle, has recently been found to be highly expressed in SMCs. In addition, although it regulates moesin expression, it

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DOI:10.14744/AnatolJCardiol.2018.35002

can also inhibit vascular SMC proliferation in vitro and after balloon injury in vivo, at least partially (23). Further, knockdown or overexpression of *BRG1* can affect H_2S-induced inhibition of the proliferation of vascular SMCs (24, 25).

In the present study, we also assessed the association between the rs1122608 SNP and several environmental factors. The data indicate that the interaction between the T allele of rs1122608 and smoking or alcohol use, or the rs1122608 CC genotype and alcohol use, may result in an increased risk of AMI. Diabetes, rs1122608, high blood pressure, age, smoking, and sex were all risk factors for AMI, while HDL-C was negatively correlated with the risk of AMI. AMI is a multifactorial disease characterized by a complex pathogenesis involving not only the individual genetic background but also lifestyle and environmental risk factors (26). Overwhelming evidence has confirmed that risk factors for AMI include smoking, high blood pressure, high blood cholesterol, lack of exercise, diabetes, obesity, excessive alcohol intake, and poor diet (27, 28). However, little is known about the combined genetic influence of rs1122608 and environmental factors. Telomere shortening has recently been suggested as a factor (29). Telomeres are specialized DNA-protein structures, located at the ends of all chromosomes, that preserve chromosome integrity and stability. In normal cells, telomeres become shorter with each cell division due to the inability of the DNA replication machinery to completely duplicate the telomeric DNA (30). Telomere length is highly variable at birth but steadily decreases with age (31). Health and longevity have been associated with telomere length in previous studies (32). Shorter leukocyte telomeres have been observed in MI cases and their offspring (33, 34). Lifestyle is well known to be among the stronger predictors of the risk of coronary heart disease and has also been reported to exert a modest effect on telomere length (35). Smoking has been associated with shorter telomeres in lean, normal-weight, and obese women (36, 37). In healthy twins, greater physical activity has been associated with longer telomeres (38). Shorter telomeres have also been observed in subjects with impaired glucose tolerance and type II diabetes in some studies (39, 40). Another study demonstrated that men with lower vitamin C intake are more likely to suffer from AMI (41). Several environmental factors have been documented to influence biological mechanisms, but relatively little is known about gene–environmental effects. Further studies are essential.

Study limitations

There were several limitations of 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 evidence to prove the association between the gene and early DT. Finally, the study did not include any data regarding the mechanism of association between the gene and AMI.

Conclusion

In conclusion, our data indicate that the mutant GT and TT genotypes and minor T allele of the BRG1 rs1122608 SNP is positively correlated with the risk of AMI. An individual carrying the mutant GT and TT genotypes or minor T allele of rs1122608 would be at 16.038 times the risk for AMI compared with an individual without those genotypes or that allele. In addition, the interactions between the minor T allele of rs1122608 and smoking or alcohol, and the rs1122608 CC genotype and alcohol, appear to increase the risk of AMI. Finally, it was verified again that diabetes, rs1122608, high blood pressure, age, smoking, and sex are risk factors for AMI, while HDL-C was negatively correlated with the risk of AMI.

Acknowledgments: This study was supported by the National Natural Science Foundation of China (No. 81560318); Guangxi medical and health suitable technology development project (No. S2017021 & No. S2017037); and Science and technology research project of Guangxi colleges and universities (No. KY2015ZD029 & No. KY2016YB099). We thank Dr. Claudia S. Copeland, Ph.D., of Carpe Diem Biomedical Writing and Editing, for scientific English editing of the manuscript.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept – W.W.; Design – Q.C., W.W.; Supervision – W.W.; Fundings – Q.C., W.W.; Materials – Z.H., D.H., T.L., F.W., J.L.; Data collection &/or processing – Z.H., D.H., T.L., F.W., J.L.; Analysis &/or interpretation – Z.H., D.H.; Literature search – T.L., F.W., J.L.; Writing – Q.C., W.W.; Critical review – Q.C., W.W.

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