



# Association of genetic polymorphisms of *SAA1* (rs12218) with myocardial infarction in a Chinese population

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**ABSTRACT.** Previous studies suggested that genetic polymorphisms of serum amyloid A (SAA) were associated with carotid atherosclerosis. However, the relationship between genetic polymorphisms of SAA and myocardial infarction (MI) remains unclear. In the present study, we analyzed a polymorphism (rs12218) in the *SAA1* gene in 840 MI patients and 840 healthy subjects by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. We found that the rs12218 CC+CT genotype was more frequent among MI patients than among healthy controls (61.1% vs 41.9%;  $P < 0.001$ ). Multivariate regression analysis showed that after adjustment for gender, age, smoking, drinking, hypertension, and diabetes, the difference remained significant ( $P < 0.001$ , odds ratio = 3.332, 95% confidence interval = 1.781-9.231). Therefore, we concluded that genetic polymorphisms of

*SAA1* may be a genetic marker of MI in the Chinese population.

**Key words:** Genetic polymorphisms; Serum amyloid A; Myocardial infarction

## INTRODUCTION

The pathogenesis of myocardial infarction (MI) is likely to comprise multifactorial disorders resulting from the inheritance of several susceptibility genes as well as multiple environmental determinants (Marenberg et al., 1994; Zee et al., 2006). Genetic epidemiology investigations have revealed that some genetic variants, including polymorphisms in apolipoprotein (Humphries et al., 2007), blood coagulation factors (Knowles et al., 2007), and inflammation factors (Crawford et al., 2006), increase the risk of coronary artery disease (CAD) and MI.

Serum amyloid A (SAA) is a sensitive acute phase protein in plasma, and is an apolipoprotein that can replace apolipoprotein A1 (apoA1) as the major apolipoprotein of high-density lipoprotein (HDL), particularly during the acute phase response. Several recent studies reported that the rs12218 polymorphism in the *SAA1* gene was associated with carotid atherosclerosis (Xie et al. 2010a), HDL-cholesterol (HDL-C) concentration (Xie et al., 2010b), and peripheral arterial disease (Xie et al., 2011). However, the relationship between SAA genetic polymorphisms and MI remains unknown. Therefore, in the present study, we investigated the relationship between rs12218 and MI in a Chinese population.

## MATERIAL AND METHODS

### Subjects

Subjects diagnosed with MI were recruited at the Sixth People's Hospital Affiliated to Shanghai Jiao Tong University from 2010 to 2013. We enrolled 840 MI patients and 840 control subjects in the present study. The diagnosis of MI was established on the basis of chest pain lasting for 20 min combined with ST-segment elevation or pathological Q waves on a surface electrocardiogram, as described previously by Xiang et al. (2009). The control subjects were selected from volunteers who came to the hospital from 2010 to 2013 for regular medical checkups and were found to be healthy.

### Genotyping

Blood samples were collected from all participants, and genomic DNA was extracted from peripheral blood leukocytes by using a DNA extraction Kit (Beijing Bioteke Co. Ltd.; China). We selected rs12218 to perform genotyping in these two groups. The genotypes were detected according to a previously described protocol (Xie et al., 2012). Briefly, genotyping was confirmed by polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP) analysis. The primers of rs12218 were as follows: sense, 5'-AACAGGGAGAATGGGAGGGTGGG-3' and antisense, 5'-GCAGGTCGGAAGTGATTGGGGTC-3'. The annealing temperature was 58°C, and the restriction enzyme used was *Bgl*I.

## Statistical analyses

Statistical analyses were carried out using SPSS version 17.0 (SPSS; Chicago, IL, USA). Hardy-Weinberg equilibrium was assessed by the chi-square test. Differences in the distribution of genotypes between MI patients and control subjects were analyzed using the chi-square test. Logistic regression analyses were used to assess the contribution of the major risk factors. Two-tailed P values <0.05 were considered to be significant.

## RESULTS

### Characteristics of study participants

As shown in Table 1, there were no significant differences in gender and age between the two groups (both  $P > 0.05$ ). However, there were significant differences in hypertension, diabetes, smoking, and hyperlipidemia between the MI patients and controls.

**Table 1.** Characteristics of the participants.

Groups	N	Gender, Male (%)	Age (years)	BMI (kg/m <sup>2</sup> )	Hypertension N (%)	Diabetes N (%)	Smoking N (%)	Hyperlipidemia N (%)
MI group	840	642 (76.42)	60.2 ± 11.1	23.9 ± 3.9	421 (50.1)	311 (37.0)	487 (58.0)	324 (37.4)
Control group	840	621 (73.92)	60.5 ± 10.9	23.1 ± 3.4	132 (15.7)	101 (12.0)	314 (37.4)	212 (25.2)
P		0.11	0.14	0.53	<0.001	<0.001	<0.001	<0.001

BMI = body mass index; MI = myocardial infarction.

### *SAA1* genotype and allele frequencies

The distribution of rs12218 genotypes was in Hardy-Weinberg equilibrium in the control group ( $P > 0.05$ ; data not shown). As shown in Table 2, the rs12218 CC+CT genotype frequency was higher in the MI group than in the control group (61.1 vs 41.9%;  $P < 0.001$ ). In addition, the C allele was more frequent among MI patients than among control subjects (32.3 vs 22.4%;  $P < 0.001$ ). After adjustment of confounding factors such as gender, age, smoking, hypertension, diabetes, and hyperlipidemia, the difference remained significant between the MI patients and control subjects [ $P < 0.001$ ; odds ratio (OR) = 3.332, 95% confidence interval (CI) = 1.781-9.231].

**Table 2.** Distributions of *SAA1* genotypes.

SNP	Group	N	Genotypes N (%)			*P value	**P value
			TT	CT	CC		
rs12218	Case	840	335 (39.90)	467 (55.60)	38 (4.50)	<0.001	0.07
	Control	840	488 (58.10)	328 (39.05)	24 (2.85)		

\*P for the dominant model and \*\*P for the recessive model.

## DISCUSSION

In this study, we found that the rs12218 polymorphism in the *SAA1* gene was associated with MI in a Chinese population. *SAA1* encodes one important inflammation factor, SAA,

which is also a kind of apolipoprotein. Therefore, *SAA1* is a candidate gene for atherosclerosis and MI. Recently, Xie and colleagues reported that the rs12218 polymorphism in the *SAA1* gene was associated with intima media thickness (Xie et al., 2010a), HDL-C (Xie et al., 2010b), the ankle-brachial index (Xie et al., 2011), and plasma uric acid levels (Xie et al., 2012), which are all related to cardiovascular disease.

Inflammation is important in the pathogenesis of atherosclerosis and ischemic heart disease. Yamada (2000) reported that the *SAA1* genetic polymorphism influences the plasma concentration of SAA. Here, we performed a case-control study to observe the relationship between the *SAA1* genetic polymorphism and MI. We found that the rs12218 CC+CT genotype was much more common in MI patients than in the control subjects. After adjustment for some potential confounding variables, the association remained significant, which indicated that the rs12218 CC+CT genotype was an independent risk factor for MI. However, the mechanism that could link *SAA1* genetic polymorphisms to MI remains unknown. The change in the plasma concentrations of HDL-C and SAA resulting from the genetic polymorphism of *SAA1* is one possible mechanism and merits further investigation.

In conclusion, the *SAA1* genetic polymorphism was associated with MI in a Chinese population.

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