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Original Article

HSG single nucleotide polymorphisms associated with serum lipids in Chinese patients with hypertension

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Abstract: Background: There was no previous study to report the association between single nucleotide polymorphisms (SNPs) of hyperplasia suppressor gene (HSG) and serum lipid traits in any population. The purpose of the present study was to firstly investigate their association. Methods and Results: A total of 674 hypertensive participants were included in the current study. We genotyped three HSG SNPs by TaqMan PCR method. Overall, subjects carrying rare type genotypes of rs2295281 and rs3753579 were obviously associated with higher triglyceride (TG). For rs1810563, subjects carrying AA genotype were associated with elevated TG. No association was found for the rest serum lipids. Subsequently participants were divided into 2 groups according to sex and body mass index. In women subgroup, low-density lipoprotein (LDL) was significantly high in C allele carriers of rs2295281 compared with TT genotype. In men, total cholesterol (TC), TG and LDL showed significant correlation with rs2295281, rs3753579 and rs1810563, respectively. No association was observed for the obese subgroup. For the case-control study, we found significant association between rs2295281 and the increased risk of hypertriglyceridemia in the recessive model (P=0.016, OR=1.85, 95% CI (1.12-3.05)) and homozygote model (P=0.035, OR=1.78, 95% CI (1.04-3.04)). Conclusion: The genetic variants of HSG may be associated with serum lipid traits (particularly TG) in Chinese patients with hypertension.

Keywords: Chinese, hyperplasia suppressor gene or HSG, lipid, SNP

Introduction

Studies have established that metabolic disorder in cholesterol, triglyceride and lipoprotein may play a key role in the onset and development of cardiovascular diseases that have seriously affected the human health [1, 2]. Determination of plasma lipid levels is multifactorial, with both genetic and environmental contributions. In many studies, genetic factor working with environmental stimuli, such as nutrition, age and physiological status, etc, has been found to exert a marked impact on the metabolism abnormality of lipids [3-5]. Studies involving genetic variation and its contribution to blood lipid level have been explored for several decades [6-8] and many gene polymorphisms have been treated as candidate determinants.

Hyperplasia suppressor gene/mitofusion-2 (HSG/Mfn2), a relatively novel gene, is located on the short (p) arm of chromosome 1 at position 36.22 [9]. HSG/Mfn2 is highly expressed in heart, brain, lung, kidney, skeletal muscle and liver. The overexpression of HSG/Mfn2 has obvious effect on the inhibition of balloon injury-induced neointimal vascular smooth muscle cells proliferation in animal's carotid arteries [9]. Beside this above function, HSG/Mfn2 plays a key role in the mitochondrial fusion, and contributes to the maintenance of mitochondrial function and morphology [10-12]. The balance between mitochondrial fission and fusion, if due to abnormal expression of HSG/Mfn2, can be disrupted, the disorder linked to energy metabolism, cell apoptosis and oxidation may be adduced and further lead to a wide range of pathological alterations including obesity, dyslipidemia, atherosclerosis or essential hypertension [13, 14]. The abnormal expression of HSG/Mfn2 was observed to be correlated with the levels of serum lipids (mainly triglyceride) in some studies [15, 16]. The relationship

between HSG/Mfn2 single-nucleotide-polymorphisms (SNPs) and essential hypertension and their possible pathogenic mechanism have been studied by our team before [17]. However, in this study, we paid particular attention to the role of the HSG/Mfn2 SNPs in serum lipids.

Since the HSG was first reported in Chinese in 2004 by Chen et al. [9], more and more SNPs within HSG have been found, and some are associated with blood pressure and Charcot-Marie-Tooth disease in genetic association studies [17, 18]. However, so far no study has been able to address the association of the HSG SNPs with serum lipids in any population. Thus, in our study, we wanted to know the underlying relationship between the HSG rs2295281, rs3753579, and rs1810563 SNPs in the coding region and serum lipid levels in the Chinese hypertensive population.

Materials and methods

Subjects

All Han Chinese subjects in the present study were identified from the hypertension clinic at Beijing Anzhen Hospital (Capital Medical University, China). Finally, 674 hypertensive patients were enrolled. Hypertension was diagnosed as the average systolic blood pressure (SBP) ≥ 140 mmHg and/or the average diastolic blood pressure (DBP) ≥ 90 mmHg and/or self-reported current use of antihypertensive medications [19]. The subjects suffering from any other diseases, such as secondary hypertension, kidney diseases, hepatic disorders, cancers, and diabetic disease, etc, were deleted. The following biochemical parameters for each individual were determined by standard laboratory methods: plasma glucose level (mmol/L), total cholesterol (TC, mmol/L), serum triglyceride (TG, mmol/L), low-density lipoprotein cholesterol (LDL, mmol/L) and high-density lipoprotein cholesterol (HDL, mmol/L). The information about blood pressure, gender, age, height and weight were interviewed or measured. Written informed consent was obtained from all subjects. This study agreed with the Declaration of Helsinki, and was approved by the Ethics Committee of Beijing Anzhen Hospital of the Capital University of Medical Sciences.

Genotyping of SNPs

Peripheral venous blood (5 ml) was taken into the iced tubes containing EDTA, and then genomic DNA was extracted from these blood samples using standard phenol-chloroform methods. The genotypes were performed using the manufacture's instruction with TaqMan assays. Primers and probes were designed and acquired from Assay-by-Design Service (Applied Biosystems). We amplified DNA samples with the help of Real-Time Polymerase Chain Reaction (PCR) technology. The thermal cycling was carried out in a GeneAmp PCR System 9700 thermal cycler (Perkin Elmer Corporation, Applied Biosystems, 850 Lincoln Centre Drive, Foster City, CA 94404, USA). The fluorescence levels of PCR products were analyzed for the differentiation of the genotypes by an ABI PRISM 7900HT Sequence Detector (Applied Biosystems). Three SNPs of HSG/Mfn2 (rs2295281, rs3753579 and rs1810563) were genotyped. All genotype determinations were performed blindly.

Statistical analysis

All results for continuous data were expressed as mean ± SD, and the level of statistical significance was defined as a $P < 0.05$. The statistical analysis was done by SPSS 18.0 (SPSS Inc, Chicago, Illinois). Hardy-Weinberg equilibrium (HWE) testing was performed by a chi-square test using a web-based program (http://ihg.gsf.de/cgi-bin/hw/hwa1.pl) if needed. One sample Kolmogorov-Smirnov test was applied to find whether TG, TC, LDL, and HDL met normal distributions. The multivariate linear regression adjusted for covariates (sex, age, BMI and glucose) were used to assess the association between each polymorphism of HSG and four lipid traits (TC, TG, LDL and HDL). Codominant, dominant, and recessive genetic models were adopted in this statistical analysis. Subgroup analysis according to sex as well as body mass index (BMI) was carried out. The group of obesity was defined as BMI ≥ 25 and non-obesity was defined as BMI < 25 according to World Health Organization recommendations for Asians [20, 21]. Finally, for the case-control study, the differences in genotype distributions and allele frequencies between groups were assessed with a chi-square test. The association of HSG SNPs with hypertriglyceridemia was determined by multivariate logistic regression adjusted for covariates (sex, age, BMI and glucose) under the five genetic models (allelic, dominant, recessive, homozygote and additive comparison). The odds ratios together

Table 1. The results for the relationship between HSG SNPs and serum lipids (mmol/L) in the whole analysis

SNPs	11	12	22	P*	P**	P***
rs2295281	TT	TC	CC			
n	85	324	255			
TC, mmol/L	5.71±3.04	5.57±2.16	5.73±4.12	0.69	0.51	0.88
TG, mmol/L	2.74±2.95	2.11±1.55	2.21±1.37	0.05	0.56	0.003
LDL, mmol/L	3.27±0.96	3.40±0.92	3.35±0.82	0.78	0.72	0.28
HDL, mmol/L	1.13±0.26	1.22±0.69	1.15±0.28	0.88	0.36	0.30
rs3753579	AA	AG	GG			
n	122	351	194			
TC, mmol/L	5.92±3.11	5.38±1.88	5.88±4.63	0.80	0.14	0.20
TG, mmol/L	2.57±2.83	2.10±1.40	2.24±1.33	0.09	0.57	0.019
LDL, mmol/L	3.33±1.04	3.34±0.86	3.41±0.82	0.32	0.34	0.53
HDL, mmol/L	1.16±0.27	1.22±0.68	1.13±0.25	0.56	0.21	0.67
rs1810563	GG	GA	AA			
n	123	332	212			
TC, mmol/L	5.45±1.67	5.66±3.72	5.71±2.83	0.60	0.71	0.63
TG, mmol/L	2.29±1.41	2.10±1.31	2.39±2.38	0.08	0.027	0.62
LDL, mmol/L	3.37±0.82	3.37±0.86	3.32±0.95	0.51	0.44	0.82
HDL, mmol/L	1.14±0.27	1.21±0.68	1.17±0.27	0.94	0.73	0.58

Abbreviations: SNPs, single-nucleotide-polymorphisms; TC, total cholesterol; TG, serum triglyceride; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol. *P, **P and ***P representing the results adjusted for sex, age, BMI and glucose in the codominant genetic model, dominant genetic model and recessive genetic model, respectively.

with their 95% confidence intervals were calculated as the final expressions.

Results

Participants' characteristics

Overall, we recruited the 674 subjects in this study. The participants had 435 men (64.5%) and 239 women (35.5%), and the mean age of the total group was 53.96 ± 11.20 years.

Among all the subjects, the successful test rate was 98.5% samples for rs2295281, 99.0% for rs3753579, and 99.0% for rs1810563. In our study, the genotype frequencies of rs2295281 were 12.8% for TT (n=85), 48.8% for TC (n=324), 38.4% for CC (n=255), and the frequency of T allele was 0.372. The genotype frequencies of rs3753579 were 18.3% for AA (n=122), 52.6% for AG (n=351), 29.1% for GG (n=194), and the frequency of A allele was 0.446. The genotype frequencies of rs1810563 were 18.4% for GG (n=123), 49.8% for GA (n=332), 31.8% for AA (n=212), and the frequency of A allele was 0.433. The genotype distribution for the three SNPs met with Hardy-Weinberg expectation (P=0.3, 0.1 and 0.7, respectively).

Association of the SNPs with four lipid traits in all subjects

The results of the relationship between the HSG SNPs and lipids in the whole population were shown in **Table 1**. In the multivariate regression analysis with sex, age, BMI and glucose as the confounding risk variables, we observed that, TG was significantly high in TT genotype of rs2295281 compare with C allele carriers. The similar result was found in AA genotype of rs3753579 compared with G allele carriers. For the remaining SNP (rs1810563), subjects carrying AA genotype were associated with higher TG values than G allele carriers. No other significant association regarding this SNP was seen under the three genetic models.

Association of the SNPs with four lipid traits in different subpopulations

The results of multivariate analysis adjusted for age, BMI and glucose in the subgroup according to sex were shown in **Table 2**. As a result, in women, LDL was significantly high in C allele carriers of rs2295281 compared with TT genotype. There were no significant association between rs3753579 and rs1810563 and lipids in women subgroup. In men, TT genotype of rs2295281 was significantly associated with higher TG values compared with C allele carriers. Similar finding was observed in AA genotype of rs3753579. Moreover, A allele carriers of rs3753579 had reduced TC and LDL compared with GG genotype. For rs1810563, G allele carriers were significantly associated with lower TG value compared with AA genotype.

Table 2. The results for the relationship between HSG SNPs and serum lipids (mmol/L) in the subgroup analysis by sex

	Women						Men					
SNPs	11	12	22	P*	P**	P***	11	12	22	P*	P**	P***
rs2295281	TT	TC	CC				TT	TC	CC			
n	30	124	80				55	200	175			
TC, mmol/L	5.72±1.89	6.05±2.66	5.72±2.46	0.78	0.48	0.67	5.71±3.54	5.27±1.72	5.74±4.70	0.44	0.20	0.73
TG, mmol/L	2.18±1.20	1.89±0.89	2.00±1.25	0.77	0.62	0.21	3.04±3.54	2.24±1.84	2.31±1.41	0.07	0.51	0.006
LDL, mmol/L	3.15±0.79	3.67±1.00	3.36±0.74	0.98	0.09	0.021	3.33±0.96	3.24±0.83	3.34±0.86	0.61	0.35	0.72
HDL, mmol/L	1.20±0.23	1.35±0.53	1.27±0.33	0.80	0.56	0.19	1.09±0.26	1.15±0.76	1.09±0.24	0.83	0.52	0.60
rs3753579	AA	AG	GG				AA	AG	GG			
n	49	123	63				73	228	131			
TC, mmol/L	6.23±2.70	5.73±2.29	5.77±2.62	0.44	0.88	0.25	5.71±3.36	5.19±1.58	5.94±5.34	0.32	0.04	0.48
TG, mmol/L	2.00±1.03	1.88±0.90	2.06±1.36	0.33	0.22	0.77	2.95±3.52	2.22±1.60	2.32±1.31	0.037	0.38	0.007
LDL, mmol/L	3.49±1.08	3.53±0.92	3.39±0.76	0.67	0.36	0.78	3.22±1.00	3.23±0.81	3.42±0.84	0.07	0.035	0.46
HDL, mmol/L	1.26±0.26	1.35±0.55	1.25±0.30	0.71	0.34	0.67	1.09±0.26	1.15±0.72	1.08±0.21	0.75	0.45	0.73
rs1810563	GG	GA	AA				GG	GA	AA			
n	36	121	81				87	211	131			
TC, mmol/L	5.52±1.43	5.76±2.24	6.20±3.12	0.20	0.21	0.45	5.42±1.77	5.60±4.35	5.41±2.60	0.68	0.64	0.85
TG, mmol/L	1.97±1.50	1.92±0.90	2.00±1.07	0.91	0.97	0.78	2.42±1.36	2.21±1.49	2.64±2.89	0.08	0.02	0.69
LDL, mmol/L	3.42±0.81	3.50±0.88	3.50±1.01	0.96	0.81	0.69	3.35±0.83	3.30±0.84	3.22±0.91	0.26	0.31	0.43
HDL, mmol/L	1.30±0.31	1.33±0.55	1.27±0.27	0.70	0.68	0.87	1.07±0.21	1.14±0.74	1.11±0.25	0.92	0.77	0.62

Abbreviations: SNPs, single-nucleotide-polymorphisms; TC, total cholesterol; TG, serum triglyceride; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol. 1 and 2 stand for rare and frequent alleles, respectively. *P, **P and ***P representing the results adjusted for age, BMI and glucose in the codominant genetic model, dominant genetic model and recessive genetic model, respectively.

Table 3. The results for the relationship between HSG SNPs and serum lipids (mmol/L) in the subgroup analysis by BMI

	Non-obese						Obese					
SNPs	11	12	22	P*	P**	P***	11	12	22	P*	P**	P***
rs2295281	TT	TC	CC				TT	TC	CC			
n	56	231	168				29	93	87			
TC, mmol/L	5.97±3.67	5.56±2.24	5.91±4.98	0.78	0.43	0.55	5.22±1.01	5.59±1.97	5.39±1.36	0.90	0.62	0.34
TG, mmol/L	2.78±3.49	1.99±1.33	2.07±1.33	0.04	0.52	0.002	2.64±1.49	2.39±1.97	2.49±1.40	0.79	0.99	0.60
LDL, mmol/L	3.21±0.91	3.39±0.92	3.33±0.82	0.61	0.86	0.20	3.38±0.90	3.45±0.93	3.38±0.83	0.86	0.71	0.85
HDL, mmol/L	1.13±0.27	1.26±0.79	1.18±0.30	0.94	0.55	0.30	1.13±0.23	1.14±0.27	1.08±0.23	0.24	0.17	0.68
rs3753579	AA	AG	GG				AA	AG	GG			
n	77	254	127				45	97	67			
TC, mmol/L	6.10±3.78	5.44±1.93	6.06±5.62	0.79	0.20	0.30	5.61±1.35	5.25±1.72	5.54±1.42	0.93	0.42	0.44
TG, mmol/L	2.45±3.03	1.98±1.34	2.15±1.38	0.19	0.89	0.032	2.77±2.48	2.42±1.51	2.41±1.23	0.29	0.53	0.25
LDL, mmol/L	3.21±1.01	3.36±0.87	3.36±0.82	0.27	0.72	0.13	3.54±1.06	3.29±0.84	3.51±0.80	0.81	0.23	0.34
HDL, mmol/L	1.17±0.28	1.26±0.77	1.16±0.26	0.77	0.28	0.43	1.15±0.24	1.11±0.26	1.08±0.23	0.29	0.39	0.36
rs1810563	GG	GA	AA				GG	GA	AA			
n	81	235	141				42	97	71			
TC, mmol/L	5.44±1.68	5.74±4.29	5.87±3.29	0.46	0.59	0.50	5.46±1.67	5.47±1.66	5.40±1.53	0.72	0.74	0.79
TG, mmol/L	2.24±1.49	1.98±1.31	2.24±2.41	0.27	0.10	0.96	2.38±1.25	2.40±1.27	2.70±2.31	0.19	0.17	0.48
LDL, mmol/L	3.39±0.84	3.35±0.86	3.28±0.95	0.33	0.37	0.51	3.34±0.77	3.44±0.86	3.40±0.97	0.90	0.88	0.68
HDL, mmol/L	1.17±0.27	1.26±0.79	1.19±0.28	0.98	0.55	0.50	1.09±0.26	1.09±0.24	1.14±0.25	0.51	0.29	0.94

Abbreviations: SNPs, single-nucleotide-polymorphisms; TC, total cholesterol; TG, serum triglyceride; LDL, low-density lipoprotein cholesterol; HDL, high-density lipoprotein cholesterol. 1 and 2 stand for rare and frequent alleles, respectively. *P, **P and ***P representing the results adjusted for sex, age and glucose in the codominant genetic model, dominant genetic model and recessive genetic model, respectively.

The results of multivariate analysis adjusted for sex, age and glucose in the subgroup according to BMI were shown in **Table 3**. All participants were then classified into the obese and non-obese subgroups. For the non-obese subgroup, a significant association was found in the TT

Table 4. Genotype distributions and allele frequencies of HSG SNPs in the case-control study

SNPs	Genotype (frequency, %)			P*	Allele (frequency, %)		P**
rs2295281	TT	TC	CC		T	C	
Hypertriglyceridemia	57 (15.4)	172 (46.5)	141 (38.1)		286 (38.6)	454 (61.4)	
Non-hypertriglyceridemia	28 (9.5)	152 (51.7)	114 (38.8)	0.07	208 (35.4)	380 (64.6)	0.22
rs3753579	AA	AG	GG		A	G	
Hypertriglyceridemia	72 (19.5)	187 (50.5)	111 (30.0)		331 (44.7)	409 (54.3)	
Non-hypertriglyceridemia	50 (16.8)	164 (55.2)	83 (27.9)	0.46	264 (44.4)	330 (55.6)	0.92
rs1810563	GG	GA	AA		G	A	
Hypertriglyceridemia	71 (19.2)	182 (49.2)	117 (31.6)		324 (43.8)	416 (56.2)	
Non-hypertriglyceridemia	52 (17.5)	150 (50.5)	95 (32.0)	0.85	254 (42.8)	340 (57.8)	0.71

Abbreviations: SNPs, single nucleotide polymorphisms. *P and **P values representing the comparison of genotype frequencies and allelic frequencies, respectively.

Table 5. The results for the relationship between SNPs and hypertriglyceridemia in the case-control study

SNPs	Model	Contrast	OR (95% CI)	P*
rs2295281				
	Allelic model	T vs. C	1.19 (0.94-1.51)	0.14
	Dominant model	(TT+TC) vs. CC	1.07 (0.77-1.48)	0.69
	Recessive model	TT vs. (TC+CC)	1.85 (1.12-3.05)	0.016
	Homozygote model	TT vs. CC	1.78 (1.04-3.04)	0.035
	Additive model	TT vs. TC vs. CC	1.20 (0.95-1.53)	0.13
rs3753579				
	Allelic model	A vs. G	1.03 (0.82-1.30)	0.78
	Dominant model	(AA+AG) vs. GG	1.03 (0.72-1.46)	0.88
	Recessive model	AA vs. (AG+GG)	0.86 (0.57-1.31)	0.49
	Homozygote model	AA vs. GG	1.11 (0.69-1.78)	0.68
	Additive model	AA vs. AG vs. GG	1.04 (0.82-1.31)	0.77
rs1810563				
	Allelic model	G vs. A	1.04 (0.83-1.31)	0.72
	Dominant model	(GG+GA) vs. AA	0.98 (0.69-1.37)	0.89
	Recessive model	GG vs. (GA+AA)	1.00 (0.67-1.52)	0.97
	Homozygote model	GG vs. AA	0.99 (0.62-1.58)	0.97
	Additive model	GG vs. GA vs. AA	0.99 (0.79-1.25)	0.94

Abbreviations: SNPs, single nucleotide polymorphisms; OR, Odds ratio; CI, confidence interval. *P-value for the results adjusted for gender, age, BMI and Glu.

genotype of rs2295281 with higher TG. AA genotype of rs3753579 was associated with higher TG value compared with G allele carriers. With reference to the obese subgroup, our data were unable to identify a significant association between the three polymorphisms and lipids.

Association of the SNPs with hypertriglyceridemia in the case-control study

To further explore the relationship between HSG SNPs and TG, we performed a case-control study and divided all into 374 hypertriglyceridemia subjects (67% men; mean age, 52.76 years; mean BMI, 27.52 kg/m^2) and 300 non-hypertriglyceridemia subjects (61% men; mean age, 55.40 years; mean BMI, 25.74 kg/m^2) according to the definition of hypertriglyceridemia. The genotype and allele frequencies were shown in **Table 4**. No significant association between the three SNPs and hypertriglyceridemia was found at the allele and genotype level (**Table 4**). In a multivariate logistic regression analysis after adjustment for gender, age, BMI and glucose, we observed that rs2295281 was significantly associated with the elevated risk of hypertriglyceridemia under the recessive model (P=0.016, OR=1.85, 95% CI (1.12-3.05)) and homozygote model (P=0.035, OR=1.78, 95% CI (1.04-3.04)) (**Table 5**). However, rs3753579 and rs1810563 showed no obvious association with the risk of hypertriglyceridemia under all genetic models in our study (**Table 5**).

Discussion

To the best of our knowledge, it appeared to be the first paper to date to investigate the asso-

ciation of the SNPs of HSG with serum lipids in the Chinese population. In the current study, the authors collected 664 participants, which all of them were Han Chinese and from Northern China showing better homogeneity. As a consequence, in the overall analysis, subjects carrying rare type (TT/AA) genotypes of rs2295281 and rs3753579 were obviously associated with higher TG. For rs1810563, subjects carrying AA genotype were associated with elevated TG. These indicated that the SNPs of HSG may be genetic markers or factors for abnormal lipid metabolism in the Chinese hypertensive population.

In this study, nearly all SNPs within HSG were in some transcript factor region. The mutation in the region can affect the transcription rate of the gene and in turn play an important role in the expression regulation of HSG/Mfn2. Our previous research found [22] that a mutation in the region caused the change of HSG/Mfn2 expression by affecting the transcript of HSG/Mfn2. The expression of HSG/Mfn2 was reported to be correlated with the levels of serum lipids in some studies [15, 16, 23]. The functional mechanism of Mfn2/HSG involving lipids mostly concentrated on the animal study rather than human, and the metabolism of TG. Chen et al. [24] found that, in Mfn2/short hairpin RNAs mice, the reduction of Mfn2/HSG expression markedly decreased the rate of fatty acid synthesis in the liver, and these mice exhibited hypertriglyceridemia, which was partially proved by another study [25]. The data by Zhao et al. [26] suggested that, the increased triglyceride content in 25-month-old rats was followed by the down-regulation of HSG/Mfn2 and the decreased mitochondrial fusion. Liu et al. [27] observed that HSG/Mfn2 can affect the cellular cholesterol transporter expression in macrophages by changing peroxisome proliferator-activated receptor-C, and the achievement of this effect was partially due to inhibit p38 mitogen-activated protein kinases and extracellular signal-regulated kinase1/2 pathway. In addition, Just as we said before, HSG/Mfn2 is a potent modulator of mitochondrial fusion with an impact on mixing of metabolites and mtDNA, organelle shape and number, and bioenergetic functionality [28]. Owing to the abnormality of HSG/Mfn2 expression, the mitochondrial fission/fusion equilibrium was unable to be established and oxidative metabolism, cell signaling, energy metabolism and apoptosis disorder may be evoked. Among them, energy metabolism and oxidation were obviously related to the lipids metabolism [29, 30]. Taken together, the precise mechanism of the HSG SNPs affecting the lipid metabolism remained unclear and additional functional studies were needed in the future.

In the subgroup analysis according to sex, the results in men involving TG were largely in accordance with the findings in the overall population, probably because the male people constituted a relatively large proportion of the total group in our study. In addition, SNPs of HSG were seemingly found to be associated with abnormality of more lipids in this subgroup. Men subjects in Chinese were more easily exposed to many high-risk factors compared with women, such as drinking, smoking, stress, etc., which was apt to result in the disorder of lipid metabolism. Due to the previous reports that the HSG/Mfn2 have some influence on lipid metabolism and obesity [23, 31], we divided the participants into the obese and non-obese subgroups. In our study, no associations were found in the obese subgroup. The limited sample size, especially subjects carrying the mutant-type alleles of the HSG SNPs, may reduce the statistical power to detect the difference. In the case-control study, we found that the frequency of the TT genotype of rs2295281 in the hypertriglyceridemia group was significantly higher than that of the non-hypertriglyceridemia group, which implied that TT genotype may be genetic risk factor for hypertriglyceridemia in the Chinese hypertensive population.

Several limitations should be mentioned when explaining the present results and continuing the related studies in future. Firstly, due to the limited sample sizes available at that time, the subgroup analysis involving the obese group can't be well done. Secondly, the analysis focusing on the detailed functional research of the HSG SNPs was not undertaken in our study and our team would take this into account as a next step. Thirdly, beside genetic background, the relationship between the HSG SNPs and lipids was also affected by many environmental factors that didn't be fully conducted in this paper, which potentially confounded the conclusions.

In conclusion, our study demonstrated a significant correlation between the HSG SNPs and serum lipids (particularly TG) in the Chinese hypertensive population. In the subsequent subgroup analysis by gender and BMI as well as case-control study, this significant association can still be seen. Further studies with larger sample size, especially studies in different races, should be applied to make clear the association between the HSG polymorphisms and serum lipids. The functional research of these SNPs on serum lipids was also required.

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Disclosure of conflict of interest

None.

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