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Original Article

The association between the *DNAH11* rs10248618 SNP and serum lipid traits, the risk of coronary artery disease, and ischemic stroke

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Abstract: Previous genome-wide association studies have shown that the rs10248618 single nucleotide polymorphism (SNP) in the dynein axonemal heavy chain 11 gene (*DNAH11*) has been associated with serum high-density lipoprotein cholesterol (HDL-C) levels. However, little is known about such association in the Chinese population. The present study was performed to clarify the association between the *DNAH11* rs10248618 SNP and serum lipid traits and the risk of coronary artery disease (CAD) and ischemic stroke (IS) in the Guangxi Han population. Genotypes of the *DNAH11* rs10248618 SNP in 1,213 unrelated patients (CAD, 600 and IS, 613) and 631 healthy controls were determined by snapshot technology. The genotypic and allelic frequencies of the SNP were significantly different between the CAD/IS patients and the controls ($P < 0.01$ for all). The CT/TT genotypes and the T allele were associated with an increased risk of CAD and IS (CAD: $P < 0.01$ for CT/TT *vs*. CC and T *vs*. C; IS: $P < 0.01$ for CT/TT *vs*. CC and T *vs*. C). The CT/TT genotypes in the healthy controls, but not in CAD or IS patients, were associated with a decreased serum HDL-C and apolipoprotein (Apo) A1 concentration. These results suggest that the *DNAH11* rs10248618 SNP is associated with the risk of CAD and IS in our study population. It is likely to increase the risk of CAD and IS by reducing serum HDL-C and ApoA1 levels.

Keywords: Dynein axonemal heavy chain 11 gene, single nucleotide polymorphism, coronary artery disease, ischemic stroke, lipids

Introduction

Atherosclerotic cardiovascular diseases, including coronary artery disease (CAD) and ischemia stroke (IS), two leading causes of mortality and disability worldwide, produce colossal health and economic burdens in the United States and globally [1]. Atherosclerosis, characterized by the damaging of arterial endothelial cells and the cumulative buildup of fatty deposits in the sub-endothelial layer [2], is a main underlying pathology of CAD and IS. CAD may share some common risk factors with IS. Behavioral/lifestyle patterns, elevated blood pressure, adverse atherogenic blood lipid levels, diabetes mellitus, and tobacco use, are known to play a role in the development of atherosclerosis [3-9].

Dyslipidemia is a major risk factor for atherosclerotic cardiovascular diseases [10]. High-density lipoprotein cholesterol (HDL-C) is involved in reverse cholesterol transport (RCT), which means that the cholesterol in the peripheral tissues is transported to the liver for excretion [11]. It is speculated that therapies which would increase the flux of cholesterol from macrophages to HDL-C would reduce atherosclerotic cardiovascular diseases. There is a strong epidemiological relationship between HDL-C and atherosclerotic cardiovascular diseases. The Tromsø Heart study is the first published epidemiological study to provide prospective evidence that the CAD risk is inversely related to HDL-C independently of low-density lipoprotein cholesterol (LDL-C), plasma triglyceride (TG) and other CAD risk factors [12].

Both CAD and IS are complex diseases, resulting from numerous additive and interacting contributions in an individual's environment and lifestyle in combination with their underly-

ing genetic architecture. Some studies have confirmed that CAD and IS have a common genetic architecture [13, 14]. We have currently searched for the susceptibility genes in serum lipid levels, CAD and IS with the positional candidate gene genotyping approach. One of the chromosomal regions that we have focused on in the present study is chromosome 7p, especially dynein axonemal heavy chain 11 (DNAH11), because this chromosomal arm is associated with CAD [15]. However, it is unknown whether those single nucleotide polymorphisms (SNPs) associated with the risk of CAD are also associated with the risk of IS.

DNAH11 consists of 13,670 nucleotides and contains a 13,569-nt ORF (GenBank accession no AJ320497). The gene is composed of 82 exons, extending over 353 kb of genomic sequence. However, *DNAH11* itself has been implicated in primary ciliary dyskinesia (PCD) [16, 17], an autosomal recessive disorder with extensive genetic heterogeneity [18], which is characterized by recurrent respiratory infections (bronchitis, rhino-sinusitis, and bronchiectasis). Half of PCD patients have situs inversus (Kartagener syndrome). Mutations in this gene have also been implicated in male sterility [19-21]. Recently, a SNP of rs10248618 in the *DNAH11* has been associated with modifications of serum HDL-C levels [22]. However, it is unknown whether the SNP associated with the HDL-C is also associated with the risk of CAD and IS. Therefore, the purpose of the present study was to detect the association between the *DNAH11* rs10248618 SNP and serum lipid traits and the risk of CAD and IS in the Chinese Han population.

Materials and methods

Cases

This study contained 1,213 unrelated patients (CAD, $n = 600$ and IS, $n = 613$). All of them were hospitalized patients in the First Affiliated Hospital, Guangxi Medical University. The CAD group included patients with stable angina and acute coronary syndrome (unstable angina, non-ST segment elevation myocardial infarction and ST segment elevation myocardial infarction). The diagnosis of CAD was based on typical angina or discomfort, electrocardiographic changes (ST-segment depression or elevation of ≥ 0.5 mm, T-wave inversion of ≥ 3 mm in ≥ 3 leads, or left bundle branch block), increases in the cardiac markers (creatinine kinase-MB and troponin T or I), as well as positive coronary angiograms (coronary stenosis ≥ 50% in at least one of the three main coronary arteries or their major branches which were reviewed by two independent angiographers who were both blinded to the clinical and genotype results) [23]. All of the IS patients received a strict neurological examination, and brain magnetic resonance imaging (MRI) was performed. The diagnosis of IS was made according to TOAST (Trial of Org 10712 in Acute Stroke Treatment) criteria, and the patients included met one or two of these criteria: large artery thrombosis and small-vessel occlusion [24]. All patients with a history of autoimmune, hematologic, neoplastic, liver, renal, thyroid, and type 1 diabetes were rejected. CAD subjects with a history of IS and IS patients with a history of CAD were also excluded.

Controls

A total of 631 healthy controls matched by age, gender, and geographical area were included. The controls were judged to be free of CAD and IS by questionnaires, medical history, and clinical examination. All individuals enrolled were from the Han population in Guangxi, China. A standard questionnaire was used to ascertain general information and the medical histories from all participants. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital, Guangxi Medical University (No. Lunshen 2009-Guike-018; Jan. 7, 2009). Informed consent was obtained from all subjects after receiving a full explanation of the study.

Genotyping and biochemical analysis

Genomic deoxyribonucleic acid (DNA) was isolated from peripheral blood leukocytes using the phenol-chloroform method. The genotyping of the *DNAH11* rs10248618 SNP was performed by the snapshot technology platform in the Center for Human Genetics Research, Shanghai Genesky Bio-Tech Co. Ltd., China. The sense and antisense primers were 5'-CCGACCAACTGTATCCCAAGC-3' and 5'-AGAATGCAGCCACAGTCAAGC-3', respectively. Before venous blood samples were obtained, all participants fasted at least 12 h. The levels of total cholesterol (TC), TG, HDL-C, and LDL-C were deter-

Table 1. General characteristics and serum lipid levels in the controls and patients

Parameter	Control	CAD	IS	P_{CAD}	P_{IS}
Number	631	600	613		
Male/Female	461/170	444/156	441/172	0.708	0.659
Age (year)	61.66±11.99	62.22±10.55	62.45±12.24	0.386	0.251
Height (cm)	155.01±7.90	164.15±6.89	161.93±15.94	0.000	0.000
Weight (kg)	54.54±9.03	64.53±10.64	65.45±18.25	0.000	0.000
Body mass index (kg/m^2)	22.62±2.83	23.88±3.22	23.52±3.61	0.000	0.000
Systolic blood pressure (mmHg)	127.62±19.46	133.16±23.39	147.21±21.74	0.000	0.000
Diastolic blood pressure (mmHg)	80.80±112.68	79.30±14.10	83.93±12.74	0.019	0.000
Pulse pressure (mmHg)	47.91±14.01	53.86±17.58	63.28±17.50	0.000	0.000
Cigarette smoking [*n* (%)]					
Nonsmoker	387 (61.3)	341 (56.7)	333 (54.3)		
Smoker	244 (38.7)	259 (43.2)	280 (45.7)	0.002	0.012
Alcohol consumption [*n* (%)]					
Nondrinker	361 (57.2)	463 (77.2)	428 (69.8)		
Drinker	270 (42.8)	137 (22.8)	185 (30.2)	0.000	0.000
Total cholesterol (mmol/L)	4.96±1.09	4.55±1.21	4.57±1.15	0.000	0.000
Triglyceride (mmol/L)	1.00 (0.67)	1.35 (0.96)	1.37 (0.89)	0.000	0.000
LDL-C (mmol/L)	2.78±0.80	2.71±1.03	2.77±0.91	0.119	0.754
HDL-C (mmol/L)	1.82±0.49	1.15±0.34	1.27±0.29	0.000	0.000
ApolipoproteinA1 (g/L)	1.43±0.27	1.03±0.34	1.02±0.19	0.000	0.000
ApoB (g/L)	0.85±0.21	0.84±0.26	0.86±0.25	0.297	0.709
ApoA1/ApoB	1.77±0.72	1.27±0.56	1.19±0.58	0.000	0.000
Hypertension [n (%)]	216 (34.2)	310 (51.7)	359 (58.6)	0.007	0.000
Hyperlipidemia [n (%)]	203 (32.2)	268 (44.7)	270 (44.0)	0.000	0.000

CAD, coronary artery disease; IS, ischemic stroke; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. P_{CAD}, CAD *vs*. controls; P_{IS}, IS *vs*. controls. The triglyceride value was presented as the median (interquartile range), the difference between CAD/IS patients and controls was determined by the Wilcoxon-Mann-Whitney test. The remaining characteristics between patients and controls were tested by the Student's unpaired *t*-test.

mined by enzymatic methods with commercially available kits (RANDOX Laboratories). The serum apolipoprotein (Apo) A1 and ApoB levels were detected by the immunoturbidimetric immunoassay.

Diagnostic criteria

The normal values in our Clinical Science Experiment Center were 3.10-5.17 mmol/L for TC, 0.56-1.70 mmol/L for TG, 0.91-1.81 mmol/L for HDL-C, 2.70-3.20 mmol/L for LDL-C, 1.00-1.78 g/L for ApoA1, 0.63-1.14 g/L for ApoB levels, and 1.00-2.50 for the ApoA1/ApoB ratio. The participants with TC > 5.17 mmol/L, and/or TG > 1.70 mmol/L were defined as hyperlipidemic [25, 26]. Hypertension was defined as a systolic blood pressure (SBP) of 140 mmHg or greater, and/or a diastolic blood pressure (DBP) of 90 mmHg or higher [27]. Drinking was based on alcohol consumption (yes or no). The individuals' ages were divided into < 60- or ≥ 60-year subgroups. Body mass index (BMI) was calculated according to the values of weight divided by height squared (kg/m^2). A BMI of < 24, 24-28, and > 28 kg/m^2 was defined as normal weight, overweight and obesity, respectively. Smoking was defined as current smoking (yes or no).

Statistical analyses

The statistical analyses were performed using the statistical software package SPSS 21.0 (SPSS Inc., Chicago, Illinois). Quantitative variables were expressed as the mean ± standard deviation (serum TG levels were presented as medians and interquartile ranges). Qualitative variables were expressed as percentages. The Handy-Weinberg equilibrium was determined using the standard goodness-of-fit test. A chi-square analysis was used to evaluate the differ-

Table 2. Genotypic and allelic frequencies and the risk of CAD and IS

Genotype/allele	Control n = 631	CAD n = 600	IS n = 613	OR (95%CI)$_{CAD}$	P_{CAD}	OR (95% CI)$_{IS}$	P_{IS}
CC	374 (59.27)	296 (49.33)	313 (51.06)	1		1	
CT	232 (36.77)	261 (43.50)	262 (42.74)	1.421 (1.125-1.795)	0.003	1.349 (1.073-3.075)	0.026
TT	25 (3.96)	43 (7.17)	38 (6.20)	2.173 (1.297-3.641)	0.003	1.395 (1.115-1.745)	0.011
x^2		14.780	9.662				
P		0.001	0.008				
CC	374 (59.27)	296 (49.33)	313 (51.06)	1		1	
CT+TT	257 (40.73)	304 (50.67)	300 (48.84)	1.495 (1.193-1.873)	0.000	1.395 (1.115-1.745)	0.004
x^2		12.245	8.477				
P		0.000	0.004				
C	980 (77.65)	853 (71.08)	888 (72.43)	1		1	
T	282 (22.35)	347 (28.92)	338 (27.57)	1.414 (1.178-1.696)	0.000	1.323 (1.102-1.587)	0.003
x^2		13.964	9.070				
P		0.000	0.003				
P_{HWE}	0.135	0.154	0.082				

HWE, Hardy-Weinberg equilibrium; CAD, coronary artery disease; IS, ischemic stroke; OR, odds ratio; CI, confidence interval. OR and 95% CI were obtained from unconditional Logistic regression model after adjusted for age, gender, body mass index, smoking status, alcohol consumption.

ence in genotype distribution between the groups. The general characteristics between the patient and control groups were tested by the Student's unpaired *t*-test. The association of genotypes and serum lipid parameters in the control group was tested by an analysis of covariance (ANCOVA). An unconditional logistic regression analysis was used to assess the correlation between the risk of CHD and IS and the genotypes. Age, gender, BMI, cigarette smoking, and alcohol consumption were adjusted for the statistical analysis. The odds ratio (OR) and 95% confidence interval (95% CI) were calculated using unconditional logistic regression analysis. Results were considered to be statistically significant if bilateral *P*-values were less than 0.05.

Results

General characteristics and serum lipid levels

The baseline characteristics of the patients with CAD or IS and the controls are shown in **Table 1**. The mean age, male to female ratio, serum LDL-C and ApoB levels were not significantly different between the controls and CAD patients and between the controls and IS patients ($P > 0.05$ for all). The values of height, weight, BMI, systolic blood pressure, pulse pressure, serum TG; the percentages of subjects who smoked cigarettes; and the prevalence of hypertension and hyperlipidemia were higher in both CAD and IS than in the control groups ($P < 0.01$ for all), but the levels of serum TC, HDL-C, ApoA1; the ratio of ApoA1 to ApoB; and the percentages of subjects who consumed alcohol were lower in both the CAD and IS patients than in control groups ($P < 0.001$ for all).

Genotypic and allelic frequencies

The genotypic and allelic frequencies of the *DNAH11* rs10248618 SNP are presented in **Table 2**. The genotype distribution of the SNP was concordant with the Hardy-Weinberg equilibrium in both cases ($P = 0.154$ for CAD and $P = 0.082$ for IS) and controls ($P = 0.135$). The frequency of the C and T alleles was 77.65% and 22.35% in the controls, 71.08% and 28.92% in the CAD patients ($P < 0.01$ for CAD *vs*. control), and 72.43% and 27.57% in the IS patients ($P < 0.01$ for IS *vs*. control); respectively. The frequencies of the CC, CT and TT genotypes were 59.27%, 36.77% and 3.96% in the controls; 49.33%, 43.50% and 7.17% in CAD patients ($P < 0.01$ for CAD *vs*. control); and 51.06%, 42.74% and 6.20% in the IS patients ($P < 0.01$ for IS *vs*. control); respectively.

DNAH11 rs10248618 SNP and the risk of CAD and IS

The T allele was associated with an increased risk of CAD (OR = 1.414, 95% CI = 1.178-1.696) and IS (OR = 1.323, 95% CI = 1.102-1.587; **Table 2**). The CT and CT/TT genotypes were

Table 3. Stratified analyses of the DNAH11 rs12670798 SNP and the risk of CAD and IS

Factors	Genotype	CAD		IS	
		OR (95% CI)	*P*	OR (95% CI)	*P*
Age					
< 60 years	CC	1		1	
	CT+TT	1.037 (0.796-1.352)	0.787	1.323 (0.947-1.847)	0.101
≥ 60 years	CC	1		1	
	CT+TT	1.544 (1.060-2.251)	0.024	1.423 (1.012-1.999)	0.042
BMI					
< 24 kg/m^2	CC	1		1	
	CT+TT	0.880 (0.602-1.286)	0.508	1.299 (0.882-1.915)	0.186
≥ 24 kg/m^2	CC	1		1	
	CT+TT	1.965 (1.468-2.630)	0.000	1.274 (0.960-1.691)	0.094
Gender					
Male	CC	1		1	
	CT+TT	1.261 (0.929-1.711)	0.156	1.183 (0.909-1.541)	0.212
Female	CC	1		1	
	CT+TT	1.105 (0.734-1.662)	0.633	2.133 (1.385-3.284)	0.001
Smoking					
No	CC	1		1	
	CT+TT	1.015 (0.708-1.454)	0.936	1.025 (0.765-1.373)	0.869
Yes	CC	1		1	
	CT+TT	2.040 (1.517-2.743)	0.000	1.591 (1.108-2.281)	0.012
Drinking					
No	CC	1		1	
	CT+TT	1.305 (0.851-2.002)	0.223	1.252 (0.918-1.707)	0.156
Yes	CC	1		1	
	CT+TT	1.345 (1.021-1.773)	0.035	1.414 (0.932-2.143)	0.103
Hypertension					
No	CC	1		1	
	CT+TT	1.296 (0.915-1.835)	0.145	1.083 (0.772-1.518)	0.644
Yes	CC	1		1	
	CT+TT	1.528 (1.127-2.072)	0.006	1.609 (1.173-2.207)	0.003

OR, odds ratio; CI, confidence interval; CAD, coronary artery disease; IS, ischemic stroke. OR and 95% CI were obtained from the unconditional logistic regression model after being adjusted for age, gender, body mass index, smoking status, alcohol consumption, and hypertension.

also associated with an increased risk of CAD (OR = 1.421, 95% CI = 1.125-1.795 for CT *vs*. CC and OR = 1.495, 95% CI = 1.193-1.873 for CT/TT *vs*. CC) and IS (OR = 1.349, 95% CI = 1.073-3.075 for CT *vs*. CC and OR = 1.395, 95% CI = 1.115-1.745 for CT/TT *vs*. CC). A stratified analysis showed an increased risk of CAD in subjects with a CT/TT genotype, mainly in those who belonged to one of the following groups: old age (OR = 1.544, 95% CI = 1.060-2.251), high BMI (OR = 1.965, 95% CI = 1.468-2.630), smokers (OR = 2.040, 95% CI = 1.517-2.743), drinkers (OR = 1.345, 95% CI = 1.021-1.773) and hypertension (OR = 1.528, 95% CI = 1.127-2.072). There was an increased risk of IS in subjects with CT/TT genotypes, mainly in those who belonged to one of the following groups: old age (OR = 1.423, 95% CI = 1.012-1.999), females (OR = 2.133, 95% CI = 1.385-3.284), smokers (OR = 1.591, 95% CI = 1.108-2.281), and hypertension (OR = 1.609, 95% CI = 1.173-2.207; **Table 3**).

Genotypes and serum lipid levels

The HDL-C and ApoA1 levels were different between the CC and CT/TT genotypes in the

Table 4. Association between rs1044925 and serum lipid levels in controls and CAD and IS patients

Genotype	n	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	ApoA1 (g/L)	ApoB (g/L)	ApoA1/ ApoB
Control								
CC	374	4.99±1.17	1.03 (0.80)	1.87±0.49	2.78±0.84	1.45±0.23	0.84±0.22	1.76±0.75
CT+TT	257	4.92±0.96	1.02 (0.77)	1.74±0.48	2.79±0.72	1.40±0.32	0.87±0.20	1.80±0.66
F		0.602	1.279	8.590	0.152	4.638	3.037	1.013
P		0.438	0.201	0.004	0.696	0.032	0.082	0.315
CAD								
CC	296	4.64±1.15	1.34 (0.94)	1.10±0.34	2.66±0.96	1.00±0.34	0.84±0.27	1.19±0.52
CT+TT	304	4.66±1.27	1.36 (0.95)	1.19±0.34	2.77±1.09	0.92±0.25	0.85±0.25	1.35±0.58
F		0.243	0.494	1.234	2.715	2.015	2.058	0.515
P		0.623	0.621	0.267	0.100	0.156	0.152	0.473
IS								
CC	374	4.49±1.21	1.37 (1.20)	1.29±0.38	2.74±0.93	1.02±0.22	0.85±0.25	1.22±0.56
CT+TT	257	4.66±1.08	1.38 (0.71)	1.25±0.17	2.79±0.88	1.03±0.15	0.87±0.25	1.16±0.60
F		0.013	0.717	0.789	0.502	0.069	0.276	0.157
P		0.908	0.474	0.095	0.479	0.793	0.599	0.692

TC, total cholesterol; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; ApoA1, apolipoprotein A1; ApoB, apolipoprotein B. The triglyceride value was presented as the median (interquartile range), and the difference between the two genotype subgroups was determined by the Wilcoxon-Mann-Whitney test. The association between the genotypes and the remaining serum lipid parameters was tested by analysis of covariance (ANCOVA).

controls ($P = 0.004$ and $P = 0.032$; respectively), but not in the CAD and IS patients (**Table 4**). The subjects with CT/TT genotypes in the controls had lower HDL-C levels than those with the CC genotype.

Discussion

DNAH11, known to be involved in the movements of cellular cilia, has been implicated in CAD. Our previous study confirmed that the *DNAH11* rs12670798 SNP is associated with CAD and IS in the Chinese population [28]. In the present study, we also showed that the genotypic and allelic frequencies of the *DNAH11* rs10248618 SNP were different between the CAD/IS patients and healthy controls. The frequency of the T allele was higher in the CAD (28.92%) and IS (27.57%) patients than in the controls (22.35%, $P < 0.01$ for each). The frequency of the TT genotype was also higher in CAD (7.17%, $P < 0.01$) and IS (6.20%, $P < 0.01$) patients than in the controls (3.96%). The CT/TT genotypes and the T allele were associated with an increased risk of CAD and IS. To the best of our knowledge, this is the first report to demonstrate that the *DNAH11* rs10248618 SNP is significantly associated with the risk of CAD and IS in the Chinese Han population. These findings suggest that the *DNAH11* rs10248618 SNP may be a susceptibility locus for CAD and IS in our study populations.

The minor allele frequency (MAF) of the *DNAH11* rs10248618 SNP was different in diverse racial/ethnic groups. The data in the International HapMap Project's database suggests that the frequency of the rs10248618 T allele was 5% in the Europeans, 22.22% in the Han Chinese in Beijing, 22.72% in the Japanese, and 36.81% in Sub-Saharan Africans. In the present study, we showed that the MAF of the T allele was 28.92% in CAD, 27.57% in IS patients and 22.35% in controls. As compared with the other populations, we found that the frequency of the rs10248618 T allele in our study populations was almost consistent with those of the International HapMap Chinese Han Beijing samples. These findings suggest that the prevalence of the *DNAH11* rs12670798 SNP might have a racial/ethnic specificity.

Cholesterol deposition is the main cause of atherosclerotic cardiovascular disease, and this lipid hypothesis can be traced back to Anitschkow's rabbit studies of about 100 years ago [29]. The epidemiological studies indicate a very strong and independent inverse associa-

tion of HDL-C with atherosclerosis [12, 30-34]. It is estimated that a 10 mg/L increase in HDL-C is associated with a 2-4% lowering of coronary death independent of LDL-C [35]. Although reverse cholesterol transport was first postulated to be a major contributor to the flux of cholesterol from macrophages to HDL-C that would reduce atherosclerotic cardiovascular disease, many other specious contributions have been disclosed. Elevated concentrations of serum HDL-C contribute to protection against cardiovascular disease through multiple mechanisms, including antiplatelet, anti-inflammatory, antioxidant, anti-apoptotic, vasodilatory activities and antithrombotic properties, as well as effects on glucose metabolism [36-43]. Recently, many studies have suggested that HDL-C is a complex of many proteins and phospholipids, with different physiological and metabolic properties. These proteins are organized into high-density lipoprotein subspecies, a lipoprotein granule system that has just been considered structural, functional, and disease-related [44-47].

The potential association between the *DNAH11* rs10248618 SNP and serum lipid profiles in humans has been evaluated in previous GWAS. It has reported a significant association between the *DNAH11* rs10248618 SNP and HDL-C levels [22]. In the current study, we found that serum HDL-C and ApoA1 levels in the control group were different among the genotypes of the *DNAH11* rs10248618 SNP, as the subjects with CT/TT genotypes had lower HDL-C and ApoA1 levels than those with the CC genotype. These results suggest that the *DNAH11* rs10248618 SNP may be a genetic marker associated with dyslipidemia in our study populations.

The interactions of the *DNAH11* rs10248618 SNP and some environmental factors on the risk of CAD and IS are not known. In the present study, stratified analyses according to gender, age, BMI, smoking, drinking, and hypertension showed that the *DNAH11* rs10248618 CT/TT genotypes were associated with an increased risk of CAD in patients with age ≥ 60 years, BMI ≥ 24 kg/m^2, smokers, drinkers and hypertension subgroups, and higher risk of IS in age ≥ 60 years, female, smokers and hypertension subgroups than in the corresponding subgroups; respectively. These findings suggest that the *DNAH11* rs10248618 SNP may interact with these parameters to influence the risk of CAD and IS. But these interactions still need to be assessed with larger sample sizes in the other populations. Our findings may provide new insights into the possible biological mechanisms associated with lipid metabolism and the risk of CAD and IS.

Limitations

Although the present study provided interesting findings about the association of the *DNAH11* rs10248618 SNP and serum lipid phenotypes and the risk of CAD or IS, several potential limitations should be acknowledged. First, compared to many GWAS and replication studies, the sample size of our study was relatively small. Therefore, further studies with larger sample sizes are needed to confirm our results. Second, although we found that the rs10248618 T allele was associated with an increased risk of CAD and IS, we did not detect an association between the rs10248618 T allele and the NADH11 enzyme activity, which is important for a functional evaluation of this SNP. Third, our study examined the serum concentration of ApoA1, an indicator that reflects the function of HDL-C, which was consistent with HDL-C. However, our study did not detect other parameters related to HDL-C function, nor did it detect factors that affected HDL-C function, such as HDL-C size, ApoCIII, blood glucose, C-reactive protein (CRP) levels and fibrinogen.

Conclusions

The present study shows that the genotypic and allelic frequencies of the *DNAH11* rs10248618 SNP were significantly different between the CAD or IS patients and the controls. The TT genotype and the T allele were associated with an increased risk of CAD and IS, especially in the subgroup of age ≥ 60 years, female (IS), BMI ≥ 24 kg/m^2 (CAD), smokers, drinkers (CAD) and hypertension. The CT/TT genotypes were also associated with a decreased serum concentration of HDL-C and ApoA1 in the healthy controls. These results suggest that the detection of *DNAH11* rs10248618 SNP may have a potential role on the genetic diagnosis of dyslipidemia and atherosclerosis-related diseases such as CAD and IS in the Chinese populations. However, larger

studies of populations with different ethnic origins are required to confirm these observations.

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Disclosure of conflict of interest

None.

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