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Association of polymorphisms of preptin, irisin and adropin genes with susceptibility to coronary artery disease and hypertension

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Abstract

Objectives: Preptin, irisin and adropin are 3 new players in energy regulation that are related body mass index, lipids, glucose and insulin levels which may affect incidence of cardiovascular diseases. The aim of the present study was to evaluate eight single nucleotide polymorphisms (SNPs) of preptin genes (rs1003483, rs1004446, rs2239681, rs680, and rs3741204), irisin (rs16835198 and rs3480) and adropin (rs2281997) gene in patients with coronary artery disease (CAD) and hypertension.

Methods: This case-control study was carried out on 372 volunteers, which were divided into 3 subgroups including: CAD patients with hypertension (CAD+H+), CAD patients with no hypertension (CAD+H-), and non-hypertensive non-CAD subjects as control group (CAD-H-) as health control. Genomic DNA from whole blood was extracted and eight SNPs were assessed using polymerase chain reaction- ligase detection reaction method.

Results: A significant difference was found in the genotype and allele frequency of preptin rs1003483 gene in CAD+H+ compared to CAD+H- groups ($P = .019$ and $P = .018$, respectively). Allele frequency of rs1003483 was significantly different between CAD+H- groups and healthy control groups ($P = .043$). There also existed a significant difference the genotype frequency of rs1004446 gene in CAD+H+ compared to CAD+H- groups ($P = .027$).

Conclusions: The findings of present study revealed that the preptin rs1003483 and rs1004446 gene polymorphism might serve as predisposing factor in CAD and hypertension.

Abbreviations: CAD = coronary artery disease, PCR = polymerase chain reaction.

Keywords: adropin, coronary artery disease, hypertension, irisin, polymorphisms, preptin

1. Introduction

Cardiovascular disease is the most common, deadly, non-infectious disease in various countries.[1] Coronary artery disease (CAD) accounts for the high morbidity and mortality rates of cardiovascular disease and annually causes more than 7 million deaths worldwide.[2] With the aging population of China, CAD has become the most common and fatal disease in this country.[3] As a primary principal health challenge worldwide, hypertension is associated with CAD development and other risk factors. Approximately 338 million Chinese are hypertensive, and this number exceeds the entire population of U.S..[4]

Diabetes, obesity, and metabolic syndrome are important CAD risk factors, and hypertension and their incidences are closely related to energy metabolism.[5] Preptin, irisin, and adropin, with 34, 43, and 112 amino acids at 3948, 4999, and 12587 Da, respectively, are associated with energy regulation. With the synthesis and secretion of these 3 peptides from different organs and body parts, their critical roles in energy regulation have been studied.[6]

Preptin derivates, such as pro-insulin-like growth factor II, are the latest discovered member of the insulin family. Preptin can elevate insulin secretion and is associated with increased insulin resistance in obesity.[7,8] Adropin is involved in lipid metabolism regulation and can affect insulin resistance.[9] Irisin can convert white adipose tissue to brown ones that store triglycerides and fatty acids and can mediate insulin resistance.[10] The relation between the levels of preptin, irisin, and adropin and cardiovascular diseases has been extensively investigated. For instance, it

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Table 1

The primers used for preptin (rs1003483, rs1004446, rs2239681, rs680, and rs3741204), irisin (rs16835198 and rs3480) and adropin (rs2281997) polymorphisms genotyping.

Peptides	SNP	Ancestor allele	Primer sequence	Product size
Preptin	rs1003483	T	F (5'-3'): ACGTTGGATGCAAGGTCAGCGCCTCGTCT	117
			R (5'-3'): ACGTTGGATGGCCCAGCATTTTACAAACCC	
	rs1004446	G	F (5'-3'): ACGTTGGATGAGCCTCAACTTCAGGGATGG	106
			R (5'-3'): ACGTTGGATGAAAGCCTCAGTGGCTTTGTG	
	rs2239681	A	F (5'-3'): ACGTTGGATGTGGATTGGAGTCCCTGTACC	99
			R (5'-3'): ACGTTGGATGGCAAATCAGCCTGAAGAGTC	
	rs680	T	F (5'-3'): ACGTTGGATGGTCCCTGAACCAGCAAAGAG	110
			R (5'-3'): ACGTTGGATGAAATTCCCGTGAGAAGGGAG	
	rs3741204	T	F (5'-3'): ACGTTGGATGTCCCATTCCCAGAGACAAAC	89
			R (5'-3'): ACGTTGGATGAATCTCTGCGCCAGAATCTC	
Irisin	rs16835198	G	F (5'-3'): ACGTTGGATGTTGGCAGATAAGGACACCAC	98
			R (5'-3'): ACGTTGGATGAGACCCTGCCTTGTAATCAC	
	rs3480	G	F (5'-3'): ACGTTGGATGTCTTGTAGACCGGAAGGAAG	98
			R (5'-3'): ACGTTGGATGTGATAAGAGCATTGGTCCCC	
Adropin	rs2281997	C	F (5'-3'): ACGTTGGATGTGCAGTCCTGAGCCTGTTG	113
			R (5'-3'): ACGTTGGATGTCTTCCCTACCTCTCTCCTC	

SNP = single nucleotide polymorphism.

was reported that serum adropin level was associated with the severity of coronary atherosclerosis, cardiac syndrome X and stable CAD.[11] Irisin was also proposed as a possible marker of macrovascular disease, including CAD.[12] Preptin levels were associated with hypertension but exhibited discrepant results for different races.[13,14] However, possible association of preptin, irisin, and adropin gene polymorphism with susceptibility to cardiovascular diseases is poorly analyzed.

This study aims to evaluate eight single nucleotide polymorphisms (SNPs) within the genes that encode preptin, irisin, and adropin in patients with CAD and/or hypertension in a Chinese population.

2. Materials and methods

2.1. Subjects

All participants were recruited from the First Peoples' Hospital of Jining between January 2016 and February 2018. A total of 263 Chinese Han patients with CAD and/or hypertension were enrolled. Diagnosis was performed by experienced cardiologists in accordance with the following significant standards: angiographic evidence of luminal diameter narrowing >50% in at least one main coronary artery or previous history of coronary artery bypass graft surgery or a history of percutaneous coronary intervention. Patients with diastolic and systolic blood pressures ≥90 and/or ≥140 mm Hg, respectively, or were taking antihypertensive drugs were defined as hypertensive. Patients with renal failure, congenital heart disease, tumors, immune system disorders, malignancies congenital heart disease, and infectious heart disease were excluded. A total of 109 healthy sex- and age-matched controls were selected from the physical examination program through clinical examination and electrocardiogram at the same period. All volunteers were divided into three subgroups including: CAD patients with hypertension (CAD+H+), CAD patients with no hypertension (CAD+H-), and non-hypertensive non-CAD subjects as control group (CAD-H-).

This study was designed in accordance with the Declaration of Helsinki and was approved by the ethics committee of First Peoples' Hospital of Jining (approval number: JY2016009). All subjects provided written informed consents.

2.2. DNA isolation and genotyping

Approximately 1 mL of venous blood was collected and purified from the subjects by using SQ Blood DNA Kit II (D0714-250, Omega Bio-Tek, Norcross) in accordance with the manufacturer's instructions. All DNA samples were genotyped using polymerase chain reaction (PCR)–ligase detection reaction (LDR). The PCR of the eight target SNPs from each participant was amplified using the primers listed in Table 1. A DNA sequencer was applied to detect the amplified PCR products and the LDR probes subjected to a multiplex LDR reaction. More than 10% of the samples were randomly selected and retested to verify the validity of this procedure, and the results from the retested samples were consistent with those from the original samples.

2.3. Statistical analysis

All genotyping results in the studied patients and controls were tested for Hardy–Weinberg Equilibrium by applying the Chi-square test ($\chi 2$ test). Demographic characteristics were compared between the case and control groups by using the Student *t* test and Chi-square. Differences in genotype distributions and allele frequencies in the cases and controls were compared between the groups for statistical significance by Chisquare statistics ($\chi 2$ test). Binary logistic regression was also applied to evaluate the independent roles of the genotypes against CAD and hypertension risk, and the results were determined via the odds ratio with a 95% confidence interval. A 2-sided *P* value below .05 was considered statistically significant. All statistical analyses were performed with the SPSS 17.0 for Windows (SPSS Inc., Chicago, IL).

3. Results

3.1. Demographics analysis

The demographic and blood pressure parameters of CAD+H+, CAD+H-, and CAD-H- are presented in Table 2. The three

Table 2

Demographics and biochemical parameters among the 3 studied groups.

Variables	CAD^+H^+(n = 135)	CAD^+H^-(n = 128)	CAD^-H^-(n = 109)	*P*-value
Age, yr	55.39 ± 7.00	54.43 ± 8.19	53.52 ± 7.75	.167
Sex (m/f)	74/61	65/63	51/58	.458
SBP (mm Hg)	148.48 ± 13.63	126.46 ± 10.94	127.71 ± 11.19	.000*
DBP (mm Hg)	88.29 ± 11.78	76.07 ± 8.73	74.61 ± 8.05	.000*
FBS (mg/dL)	6.37 ± 2.04	5.89 ± 1.29	–	.072
TC (mg/dL)	4.46 ± 1.03	4.72 ± 1.05	–	.046*
LDL-c (mg/dL)	2.45 ± 0.74	2.55 ± 0.77	–	.278
HDL-c (mg/dL)	1.16 ± 0.30	1.26 ± 0.39	–	.018*
VLDL-c (mg/dL)	0.70 ± 0.46	0.57 ± 0.30	–	.010*
TG (mg/dL)	1.71 ± 1.36	1.21 ± 0.62	–	.000*

CAD+H+ = coronary artery disease with hypertension, CAD+H− = coronary artery disease without hypertension, CAD−H− = control, DBP = diastolic blood pressure, FBS = Fasting Blood Sugar, HDL-c = High-density lipoprotein cholesterol, LDL-c = Low-density lipoprotein cholesterol, SBP = systolic blood pressure, TC = Total cholesterol, TG = Triglyceride, VLDL-c = Very low-density lipoprotein cholesterol. Continuous and categorical values are presented as mean ± SD and number, respectively.

* Significant difference ($P < .05$).

groups were similar in terms of age and sex distribution ($P = .167$ and $P = .458$, respectively). However, significant differences were observed regarding the mean SBP and DBP ($P \leq .001$) among the three groups. The clinical and biochemical parameters of the case groups (CAD+H+ and CAD+H-) and the control group (CAD-H-) are also shown in Table 2. Significant differences on total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), very low-density lipoprotein cholesterol (VLDL-c), and triglyceride (TG) were observed among the 2 case groups and the controls ($P = .046$, $P = .018$, $P = .010$, and $P \leq .001$, respectively). No differences were found for fasting blood sugar (FBS) and low-density lipoprotein cholesterol (LDL-c).

3.2. Genotype and allele frequencies distribution among 3 groups

The observed preptin (rs1003483, rs1004446, rs2239681, rs680, and rs3741204), irisin (rs16835198 and rs3480), and adropin gene (rs2281997) genotype frequencies were in accordance with the Hardy–Weinberg equilibrium in the 3 study groups.

The details of genotype and allele of eight gene polymorphism frequency distribution were compared, and the results are presented in Table 3. Significant differences were found in the genotype and allele frequency of the preptin polymorphism rs1003483 in CAD+H+ compared with those of the CAD+H- groups ($P = .019$ and $P = .018$, respectively). Similarly, the genotype of the preptin polymorphism rs1004446 was significantly different between the CAD+H+ and CAD+H- groups ($P = .027$). Another significant difference was found regarding the allele frequency of rs1003483 between CAD+H- groups and healthy control groups (CAD-H-) ($P = .043$). The genotype and allele frequencies of the rs2239681 (preptin), rs680 (preptin), rs3741204 (preptin), rs16835198 (irisin), rs3480 (irisin), and rs2281997 (adropin) SNPs showed no differences among CAD and/or hypertensive patients.

The association of rs1003483 and rs1004446 genotypes with FBS, TC, LDL-c, HDL-c, VLDL-c, and TG (mg/dl) was studied, and the results are shown in Table 4. FBS concentrations for rs1003483 were significant higher in the TT genotype group than in the TG genotype group in patient groups ($P = .015$). For rs1004446, the TG serum level was significantly higher in the GG genotype patients compared with that in the GA genotype patients ($P = .037$)

3.3. Results of binary regression models

Table 5 presents the results of data analysis by binary regression mode. No significant differences were observed in the studied polymorphic genotypes and the risk of CAD and hypertension.

4. Discussion

Maintaining energy balance over time is vital to achieve and sustain the health of an individual. Many peptide hormones of the endocrine system play a key role in maintaining energy balance. When energy input is greater than expenditure, the balance is positive; otherwise, the balance is negative. The physical indicator changes with energy imbalance.[15,16] The main indicators, including body mass index (BMI), lipids, glucose, and insulin levels, can be affected by energy metabolisms and influence the incidence of hypertension and CAD.[5] Preptin, adropin, and irisin are the three new players in energy regulation, and the association of their gene polymorphisms with susceptibility to CAD and hypertension was studied in this work. This association in the Chinese population has never been reported.

Adropin is a 4.9 kDa amino acid secreted peptide that is mainly expressed in the liver, brain, and many peripheral tissues. Adropin mainly ameliorates the regulation of lipid metabolism and glucose homeostasis and controls energy balance, insulin resistance, and endothelial functions, all of which are associated with obesity.[9,17] Irisin is a 112 amino acid exercise-induced peptide that was first reported in 2012 by Bostrom in Harvard University.[18] This peptide is secreted principally in the heart and skeletal muscles and other peripheral tissues, including salivary glands, kidney and liver. Irisin regulates adipose tissue, can induce the browning adipose tissue, and plays a key protective role in the development of obesity-related diseases, such as insulin resistance, arteriosclerosis, and type 2 diabetes.[19]

Adropin and irisin are related to cardiovascular diseases. The former is a potential protective regulator of atherogenesis and cardiovascular diseases.[20,21] Zhao et al found that serum adropin level is inversely associated with the severity of coronary atherosclerosis and serum level of homocysteine.[22] Celik et al reported that the serum adropin is decreased in patients with cardiac syndrome X and stable CAD.[11] Plasma adropin level is an independent indicator of hypertension.[23,24] Individuals at risk for cardiovascular disease exhibit some type of irisin resistance.[25,26] Therefore, irisin may be a possible marker of

Table 3

Genotypic and allelic distribution of preptin (rs1003483, rs1004446, rs2239681, rs680, and rs3741204), irisin (rs16835198 and rs3480) and adropin (rs2281997) polymorphisms among the 3 studied groups.

	1	2	3	*P*-value			
SNP	**CAD^+H^+(n = 135)**	**CAD^+H^-(n = 128)**	**CAD^-H^-(n = 109)**	**1vs 2**	**1vs 3**	**2 vs 3**	**1and 2 and 3**
Preptin							
rs1003483							
TT	65 (48.2)	40 (31.3)	45 (41.3)	.019*	.136	.092	.054
TG	52 (38.5)	67 (52.3)	55 (50.5)				
GG	18 (13.3)	21 (16.4)	9 (8.2)				
Allele T	182 (67.4)	147 (57.4)	145 (66.5)	.018*	.835	.043*	.075
Allele G	88 (32.6)	109 (42.6)	73 (33.5)				
rs1004446							
GG	79 (58.5)	62 (48.4)	62 (56.9)	.027*	.714	.198	.196
GA	43 (31.9)	60 (46.9)	39 (35.8)				
AA	13 (9.6)	6 (4.7)	8 (7.3)				
Allele G	201 (74.4)	184 (72.9)	163 (74.8)	.506	.934	.478	.883
Allele A	69 (25.6)	72 (28.1)	55 (25.2)				
rs2239681							
AA	57 (42.2)	56 (43.8)	41 (37.6)	.335	.622	.508	.544
AG	56 (41.5)	59 (46.1)	52 (47.7)				
GG	22 (16.3)	26 (20.3)	16 (16.7)				
Allele A	170 (63.0)	145 (56.6)	134 (61.5)	.139	.735	.287	.420
Allele G	100 (37.0)	111 (43.4)	84 (38.5)				
rs680							
TT	52 (38.5)	34 (26.6)	33 (30.2)	.118	.360	.694	.389
TC	64 (47.4)	72 (56.2)	61 (56.0)				
CC	19 (14.1)	22 (17.2)	15 (13.8)				
Allele T	168 (62.2)	140 (54.7)	127 (58.3)	.080	.373	.435	.288
Allele C	102 (37.8)	116 (45.3)	91 (41.7)				
rs3741204							
TT	87 (64.4)	73 (57.0)	69 (63.3)	.255	.765	.588	.169
TC	38 (28.2)	48 (37.5)	34 (31.2)				
CC	10 (7.4)	7 (5.5)	6 (5.5)				
Allele T	212 (78.5)	194 (75.8)	172 (78.9)	.455	.919	.420	.827
Allele C	58 (21.5)	62 (24.2)	46 (21.1)				
Irisin							
rs16835198							
GG	31 (23.0)	30 (23.4)	28 (25.7)	.956	.885	.893	.987
GT	72 (53.3)	66 (51.6)	56 (51.4)				
TT	32 (23.7)	32 (25.0)	25 (22.9)				
Allele G	134 (49.6)	126 (49.2)	112 (51.4)	.925	.701	.662	.922
Allele T	136 (50.4)	130 (50.8)	106 (48.6)				
rs3480							
GG	12 (8.9)	11 (8.6)	14 (12.8)	.853	.590	.423	.699
GA	42 (31.1)	36 (28.1)	34 (31.2)				
AA	81 (60.0)	81 (68.3)	61 (56.0)				
Allele G	66 (24.4)	58 (22.6)	62 (28.4)	.629	.318	.149	.538
Allele A	204 (75.63)	198 (77.4)	156 (71.6)				
Adropin							
rs2281997							
CC	102 (75.6)	95 (74.2)	83 (76.1)	.201	.287	.723	.387
CT	30 (22.2)	33 (25.8)	26 (23.9)				
TT	3 (2.2)	0 (0.0)	0 (0.0)				
Allele C	234 (75.3)	221 (87.3)	192 (88.1)	.725	.561	.809	.822
Allele T	36 (75.3)	31 (12.7)	26 (11.9)				

CAD+H- = coronary artery disease, CAD-H- = control, H+CAD+ = coronary artery disease and hypertension.
* Significant difference ($P < .05$).

macrovascular disease in people with T2DM because it is reduced in people with T2DM and macrovascular complications, such as CAD.[12] Eugen Brailoiu et al reported that irisin evokes bradycardia by activating the cardiac-projecting neurons of nucleus ambiguous.[27] In the present work, no association was found for irisin (rs16835198 and rs3480) and adropin (rs2281997) gene polymorphisms with susceptibility to CAD and hypertension. This finding may be ascribed to the small sample size or the limited coverage of the selected SNPs for the genomes coding irisin and adropin.

Table 4

Association of rs1003483 and rs1004446 genotypes with some biochemical parameters levels in the case groups.

				P value			
	1	2	3	1vs 2	1vs 3	2 vs 3	1and 2 and 3
rs1003483	TT	TG	GG				
FBS (mg/dL)	6.45 ± 2.19	5.87 ± 1.32	6.09 ± 1.27	.015*	.331	.363	.041*
TC (mg/dL)	4.60 ± 1.03	4.50 ± 1.04	4.83 ± 1.07	.511	.222	.089	.229
LDL-c (mg/dL)	2.47 ± 0.74	2.50 ± 0.76	2.57 ± 0.80	.728	.456	.618	.756
HDL-c (mg/dL)	1.19 ± 0.31	1.20 ± 0.37	1.29 ± 0.39	.903	.118	.185	.295
VLDL-c (mg/dL)	0.66 ± 0.45	0.63 ± 0.35	0.62 ± 0.38	.617	.682	.917	.847
TG (mg/dL)	11.58 ± 1.46	1.42 ± 0.77	1.31 ± 0.69	.287	.268	.438	.344
rs1004446	GG	GA	AA				
FBS (mg/dL)	6.25 ± 1.97	5.97 ± 1.33	6.22 ± 1.77	.209	.955	.468	.443
TC (mg/dL)	4.65 ± 1.08	4.52 ± 0.99	4.50 ± 1.03	.338	.554	.919	.581
LDL-c (mg/dL)	2.52 ± 0.77	2.50 ± 0.73	2.40 ± 0.77	.831	.532	.595	.812
HDL-c (mg/dL)	1.22 ± 0.35	1.19 ± 0.33	1.24 ± 0.43	.454	.820	.537	.701
VLDL-c (mg/dL)	0.67 ± 0.46	0.58 ± 0.25	0.70 ± 0.25	.077	.798	.124	.177
TG (mg/dL)	1.60 ± 1.37	1.30 ± 0.58	1.48 ± 0.79	.037*	.730	.220	.105

FBS = fasting blood sugar, HDL-c = high-density lipoprotein cholesterol, LDL-c = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, VLDL-c = very low-density lipoprotein cholesterol. Continuous and categorical values are presented as mean ± SD and number, respectively.

* Significant difference ($P < .05$).

Preptin is a 34 (MW 3948 Da) amino acid peptide that is primarily synthesized in pancreatic beta cells pancreas along with insulin, amylin, and pancreastatin. Preptin is the energy balance regulation molecule in the "beta TC6-F7 beta-cells" of rats as reported by Bucham as early as 2001. Unfortunately, this topic has been rarely studied. The physiological amplifier of glucose-mediated insulin secretion is the most important function of preptin,[28] and preptin gene polymorphisms are associated with the risk of diseases. For example, rs1003483 and rs1004446 are notably associated with high myopia, ovarian cancer, and endometrial cancer in different races.[29–31] Preptin is involved in the development of cardiovascular disease. Cai et al reported that plasma preptin levels are decreased in patients with essential hypertension in a Chinese population,[13] whereas Soha found that an increase in preptin level is associated with hypertension among Egyptians.[14] The contradictory results implied us that ethnic differences about the influence of preptin level exist on the incidence of hypertension, but a link between preptin level and hypertension has been found. Our study also uncovered significant differences for the genotype frequencies rs1003483 and rs1004446 and allele frequencies for rs1003483 of preptin between CAD group with and without hypertension. The results

Table 5

Association of preptin rs1003483, rs1004446, rs2239681, rs680 and rs3741204, irisin rs16835198 and rs3480, and adropin rs2281997 polymorphic genotypes and the risk of CAD and hypertension with binary regression.

	Group			
	CAD^+H^+ vs CAD^-H^-		CAD^+H^- vs CAD^-H^-	
Model of inheritance	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)
Preptin				
rs1003483				
TT vs (TG+GG)	.493	0.681 (0.227–2.004)	.093	2.275 (0.871–5.940)
rs1004446				
GG vs (GA+AA)	.852	0.902 (0.304–2.676)	.412	1.538 (0.550–4.301)
rs2239681				
AA vs (AG+GG)	.467	1.684 (0.413–6.861)	.282	0.530 (0.166–1.686)
rs680				
TT vs (TC+CC)	.210	0.557 (0.223–1.390)	.818	0.895 (0.348–2.300)
rs3741204				
TT vs (TC+CC)	.749	1.217 (0.365–4.053)	.961	0.972 (0. 316–2.992)
Irisin				
rs16835198				
GG vs (GT+TT)	.964	0.983 (0.469–2.060)	.773	0.893 (0.416–1.919)
rs3480				
GG vs (GA+AA)	.417	1.526 (0.550–4.237)	.366	1.633 (0.564–4.728)
Adropin				
rs2281997				
CC vs (CT+TT)	.839	1.065 (0.582–19.47)	.651	1.154 (0.620–2.149)

CAD+H+ = coronary artery disease with hypertension, CAD+H− = coronary artery disease without hypertension, CAD−H− = control, CI = confidence interval.

indicate the different genotype and allele frequencies of preptin may also be involved in the hypertension progression among patients with CAD by regulating the preptin levels.

We found the association of different allele frequencies of preptin (rs1003483) with susceptibility to CAD compared with the healthy control in this study. This result was consistent with that of Li's research results from the Chinese. The findings showed that circulating preptin is increased in patients with positive coronary calcification and can independently predict coronary calcification, which is a specific feature of coronary CAD.[32] We assumed that rs1003483 polymorphism was also a CAD marker; however, this finding must be further verified.

Preptin also plays a fundamental role in insulin secretion, which affects the blood sugar levels and other biochemical parameters. The combination of the above findings regarding the association of the polymorphisms of preptin (rs1003483, rs1004446) with susceptibility to CAD and hypertension motivated us to study the association of rs1003483 and rs1004446 genotypes with various biochemical parameter levels. We found that the FBS levels were significantly different in different rs1003483 genotypes of patients with CAD, implying that the rs1003483 may be a critical gene for preptin to increase or decrease blood glucose level by regulating insulin secretion. Another important finding of this study showed that TG level was significantly higher in rs1004446 GG genotype than that in rs1004446 GA genotype, whereas the frequency of the GG genotype in CAD+H+ is significantly higher than that in CAD+H- patients, indicating rs1004446 polymorphism may be a possible genetic susceptibility factor for hypertension in patients with CAD patients altering TG levels. Furthermore, study in Turkey revealed that preptin levels increase with high BMI,[33] and triglyceride glucose-BMI is a simple and clinically useful surrogate marker for insulin resistance. The genetic polymorphism of preptin may be important on regulating TG level, which was a risk factor for hypertension and CAD susceptibility.

This research has some limitations. First is the small sample size. Future studies must be performed with a large sample size to obtain persuasive results. Second, we failed to acquire enough data, including the BMI of the volunteers, the concentrations of preptin, irisin, and adropin, which are crucial indicators closely related to the functions of these peptides, because of various factors. Thus, we cannot assess the relationship of polymorphism and some of these data. Future studies must focus on collecting data to offer support for a profound conclusion

5. Conclusion

To the best of our knowledge, this study first proposed a potential influence of preptin polymorphism on CAD and hypertension susceptibility in a Chinese population. The findings suggest that further studies must be conducted in different racial and ethnic groups with large sample sizes.

Author contributions

Funding acquisition: Pei Jiang, Wenxiu Han.
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Writing – original draft: Haidong Wang.
Writing – review and editing: Pei Jiang, Yujin Guo.

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