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Research Article

The Impact of *CYP24A1* Polymorphisms on Hypertension Susceptibility

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Keywords
CYP24A1 · Hypertension · Case-control study · Genetic variations · Risk

Abstract
Background: Hypertension is one of the leading causes of human death and disability. *CYP24A1* regulates vitamin D activity and is closely linked to hypertension. However, the relationship between *CYP24A1* polymorphisms and hypertension risk remains unclear. ***Methods:*** This case-control study included 503 hypertensive patients and 498 healthy controls from the Chinese Han population. The genotypes of *CYP24A1* polymorphisms were detected using the Agena MassARRAY method. The association between genetic variations of *CYP24A1* and hypertension risk was evaluated with odds ratios (OR) and 95% confidence intervals (CI) in genetic models. ***Results:*** We found that rs56229249 of *CYP24A1* significantly decreased the hypertension risk in homozygote (OR 0.51, 95% CI 0.29–0.91, $p = 0.022$) and recessive models (OR 0.51, 95% CI 0.29–0.91, $p = 0.023$). Further stratification analyses indicated that hypertension risk is related to age and sex, rs2762934 polymorphism increases hypertension risk among younger subjects (<61 years), and rs1977297 influences the risk of hypertension among older subjects (≥61 years). In addition, rs2762940 is related to hypertension risk in men, and rs56229249 is a protective factor against hypertension in women. ***Conclusions:*** Our study suggests that genetic variations of the *CYP24A1* gene were significantly associated with susceptibility to hypertension in the Chinese population.

Introduction

Hypertension is the most common disease that affects human beings worldwide, accounting for 2.5 million deaths (27.5% of total deaths) in 2013 in China [1, 2]. Compared with healthy subjects, individuals with a high blood pressure (BP) stand a higher risk of some

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diseases such as stroke, coronary heart disease (CHD), heart failure, and kidney disease [3, 4]. The complex mechanisms of BP regulation are determined by tight interactions between various genetic and environmental factors [5, 6]. Approximately 30–70% variability in human hypertension is attributed to multiple genetic factors [7].

CYP24A1 (cytochrome P450 family 27 subfamily A member 1) is a gene located on chromosome 20 (q13.2) encoding the primary catabolic enzyme for circulating 1,25-dihydroxyvitamin D and 25-hydroxyvitamin D [8]. *CYP24A1* is involved in regulating the level of vitamin D. The role of vitamin D in the etiology of hypertension and cardiovascular disease has been increasingly identified [9, 10]. Previous studies indicated that vitamin D deficiency can lead to hypertension [11]. *CYP24A1*, as a gene in the vitamin D pathway, showed significant association with systolic BP, diastolic BP, or mean arterial pressure [12]. *CYP24A1* polymorphisms may modify the effect of vitamin D on BP. It has revealed that inactivating mutations of the *CYP24A1* gene in individuals are associated with the level of 1,25-dihydroxyvitamin D and parathyroid hormone (PTH) [13], hypercalcemia, hypercalciuria [14], kidney disease [15], but little research has been conducted on *CYP24A1* polymorphisms for influencing hypertension risk in the Chinese Han population. To further address the role of *CYP24A1* in hypertension development, we conducted a case-control study to investigate whether genetic variants in *CYP24A1* are related to hypertension risk.

Methods

Study Participants

The study consisted of 503 hypertensive subjects (303 males and 200 females) and 498 healthy controls with normotension (298 males and 200 females), who were recruited from the Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China. Hypertension was defined as a seated systolic and/or diastolic BP >140 and/or 90 mm Hg in at least two separate measurements by professional physicians. All hypertension patients had primary hypertension. Patients who had hypertension treatment with medications, secondary hypertension, pregnancy, inflammation, or other autoimmune diseases were excluded from this study. The control group consisted of subjects without hypertension, diabetes mellitus, tumors, inflammation-related diseases, cardiovascular diseases, or other obvious diseases. The clinical characteristics, including urea, creatinine, uric acid (UA), and lipid profile, were collected from their medical records.

Selection of Single Nucleotide Polymorphisms and Genetic Analysis

The selection of human *CYP24A1* gene single nucleotide polymorphisms (SNPs; rs2762934, rs1977297, rs2762940, rs4809958, rs56229249, and rs2585428) was based on previous studies [16, 17] and the data from the 1000 Genomes Project. Blood samples were collected from all participants and were stored in EDTA-containing vacutainers. Genomic DNA was extracted from whole blood using the GoldMag Mini Purification Kit (GoldMag Co. Ltd., Xi'an, China). Genotyping was performed using the MassARRAY iPLEX Gold Assay (Agena Bioscience, San Diego, CA, USA) [18]. The primer sequences used for genotyping the *CYP24A1* polymorphisms are shown in online supplementary Table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000503925).

Statistical and Bioinformatics Data Analyses

Statistical analysis was performed using SPSS 18.0 for Windows (SPSS, Chicago, IL, USA). Continuous variables are expressed as the mean ± standard deviations (SD) and a *t* test was performed to compare the differences in these variables between all participants. Categorical

variables were assessed by χ^2 test. In the control group, genotype distributions for each SNP were analyzed using the χ^2 test to see if they deviated from Hardy-Weinberg equilibrium. We assessed the association between *CYP24A1* polymorphisms and hypertension by odds ratios (OR) with 95% confidence intervals (CI) using logistic regression analysis [19]. Multiple models were analyzed by PLINK software, including homozygote, heterozygote, dominant, recessive, and additive models [18]. Haplotype analysis and linkage disequilibrium (LD) were evaluated by the PLINK software. Besides that, we used HaploReg v.4.1 (https://pubs.broadinstitute.org/mammals/haploreg/haploreg.phpto) to predict the possible functions on these *CYP24A1* SNPs. All of the reported *p* values are based on 2-sided tests, and $p < 0.05$ was considered to be statistically significant.

Results

Basic Characteristics of the Subjects

The characteristics for all study subjects are summarized in Table 1. The mean ages of hypertensive cases and healthy controls were 63.05 ± 10.81 and 60.69 ± 6.38 years, respectively. No significant difference was observed between the two groups in regard to sex, urea, triglyceride, total cholesterol, and high-density lipoprotein cholesterol. However, the values of creatinine, UA, and low-density lipoprotein cholesterol in the patient group were significantly different compared with those in the control group. The smoking and drinking status of the two groups are presented in Table 1. Among the patient group, 291 individuals (58%) had CHD and 202 individuals (40%) had cerebral infarction.

Genotyping and Candidate SNP Details

Six SNPs in the *CYP24A1* gene (rs2762934, rs1977297, rs2762940, rs4809958, rs56229249, and rs2585428) were successfully genotyped. The details of these candidate SNPs are shown in Table 2. All studied variants complied with the Hardy-Weinberg equilibrium ($p > 0.05$). Moreover, each selected SNP had more than 5% minor allele frequency in the Chinese population. However, there were no strong relationships between *CYP24A1* polymorphisms and hypertension risk in the allele model ($p > 0.05$). We also found that candidate SNPs were related to the regulation of enhancer histone marks, DNAse, proteins bound, and motifs changed by HaploReg (version 4.1).

Association of the Candidate SNPs with Hypertension

As shown in Table 3, homozygous rs56229249 variants had a significantly decreased risk of hypertension (OR 0.51, 95% CI 0.29–0.91, $p = 0.022$) compared to subjects with homozygous wild-type alleles. The SNP rs56229249 was also associated with a significantly lower risk of hypertension in a recessive model (OR 0.52, 95% CI 0.29–0.91, $p = 0.023$). However, no significant association was detected between the remaining 5 SNPs and hypertension risk in the Chinese population ($p > 0.05$).

Association of the Candidate SNPs with Hypertension in Stratified Subgroups

In Table 4, the genotype AG of SNP rs2762934 is associated with an increased risk of hypertension in the younger subgroup (age <61 years; OR 1.96, 95% CI 1.18–3.27, $p = 0.010$). For subjects aged 61 years or older, rs1977297 was associated with a higher risk of hypertension in multiple models (allele: OR 1.35, 95% CI 1.05–1.73, $p = 0.018$; dominant: OR 1.44, 95% CI 1.01–2.06, $p = 0.046$; additive: OR 1.35, 95% CI 1.02–1.78, $p = 0.034$). Moreover, a significant difference in the distribution of genotype AC was identified between the hypertensive and healthy men (OR 1.42, 95% CI 1.01–2.00, $p = 0.041$). Women who had

Table 1. Characteristics of hypertension patients and healthy controls

	Hypertensive cases (*n* = 503)	Healthy controls (*n* = 498)	*p*
Age	63.05±10.81	60.69±6.38	**<0.001**
≥61 years	300 (60)	282 (57)	
<61 years	203 (40)	216 (43)	
Sex			0.949
Male	303 (60)	298 (60)	
Female	200 (40)	200 (40)	
Urea	5.50±2.26	7.03±21.29	0.110
Creatinine	77.26±24.62	68.06±34.36	**<0.001**
Uric acid, μmol/L	289.04±97.88	327.78±81.56	**<0.001**
TG, mmol/L	1.68±1.29	1.78±1.21	0.284
TC, mmol/L	18.53±327.32	4.85±5.48	0.466
HDL, mmol/L	1.10±0.24	1.09±0.31	0.588
LDL, mmol/L	2.56±0.72	1.86±0.83	**<0.001**
Smoking status			
Yes	105 (21)	103 (21)	
No	45 (9)	186 (37)	
Absent	343 (70)	209 (42)	
Drinking status			
Yes	66 (13)	97 (19%)	
No	92 (18)	180 (36	
Absent	345 (69)	221 (45)	
CHD			
Yes	291 (58)		
No	212 (42)		
Cerebral infarction			
Yes	202 (40)		
No	301 (60)		

Data are presented as the mean ± SD or *n* (%). Bold *p* values are significant. HDL, high-density lipoprotein; LDL, low-density lipoprotein; CHD, coronary heart disease.

rs56229249-G were less likely to suffer from hypertension (OR 0.60, 95% CI 0.43–0.83, $p = 0.002$). In the female subgroup, there was also a strong link between rs56229249 and hypertension susceptibility in genetic models (codominant: OR 0.23, 95% CI 0.09–0.59, $p = 0.003$; dominant: OR 0.60, 95% CI 0.40–0.90, $p = 0.015$; recessive: OR 0.26, 95% CI 0.10–0.67, $p = 0.005$; additive: OR 0.59, 95% CI 0.42–0.82, $p = 0.002$). No notable relationships of rs4809958 and rs2585428 with hypertension risk were identified in the stratified subgroups, so we have not provided these data. We subsequently performed an analysis on *CYP24A1* polymorphisms and hypertension in the cardiovascular disease subgroups. As shown in online supplementary Table 2, rs56229249 of *CYP24A1* might be associated with coexisting hypertension and CHD.

Haplotypes and LD pattern

We further conducted the LD and haplotypes analyses on the *CYP24A1* polymorphisms. It revealed two blocks (block 1: rs2762934 and rs1977297; block 2: rs2762940 and rs4809958) in *CYP24A1* (Fig. 1). The association between the haplotype of *CYP24A1* and hypertension susceptibility is presented in Table 5. No significant association was found.

CYP24A1 Polymorphisms and Clinical Factors

In online supplementary Table 3, we analyzed the association between genotypes of *CYP24A1* polymorphisms and clinical factors. Hypertension patients with different genotypes

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Table 2. *CYP24A1* polymorphisms and their putative functional roles

SNP	Location: position	Alleles	MAF cases	MAF controls	OR (95% CI)	*p*	HWE *p*	HaploReg
rs2762934	Chr20: 54154722	A/G	0.110	0.103	1.07(0.80–1.42)	0.656	0.087	Enhancer histone marks, DNAse, proteins bound, motifs changed
rs1977297	Chr20: 54157940	C/T	0.332	0.305	1.13(0.94–1.37)	0.200	0.751	DNAse, proteins bound, motifs changed
rs2762940	Chr20: 54165411	A/C	0.303	0.295	1.04(0.86–1.26)	0.696	0.236	DNAse, motifs changed
rs4809958	Chr20: 54165899	G/T	0.346	0.356	0.96(0.79–1.15)	0.623	0.379	DNAse, motifs changed
rs56229249	Chr20: 54170249	A/G	0.225	0.256	0.84(0.69–1.04)	0.106	0.345	Enhancer histone marks, DNAse, proteins bound, motifs changed
rs2585428	Chr20: 54170358	A/G	0.416	0.442	0.90(0.75–1.07)	0.235	0.469	Enhancer histone marks, DNAse, proteins bound

SNP, single nucleotide polymorphism; MAF, minor allele frequency; OR, odds ratio; CI, confidence interval; HWE, Hardy-Weinberg equilibrium.

Table 3. Association between genotypes of *CYP24A1* and hypertension susceptibility

SNP	Case[a]	Control[a]	Homozygote		Heterozygote		Dominant model		Recessive model		Additive model	
			OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
rs2762934	394/106/2	404/85/9	0.25 (0.05–1.18)	0.081	1.29 (0.94–1.78)	0.119	1.20 (0.87–1.63)	0.265	0.24 (0.05–1.13)	0.070	1.09 (0.81–1.45)	0.577
rs1977297	226/219/57	236/212/44	1.34 (0.87–2.08)	0.186	1.05 (0.80–1.37)	0.726	1.10 (0.85–1.41)	0.463	1.31 (0.86–2.00)	0.203	1.12 (0.92–1.35)	0.254
rs2762940	242/217/44	253/196/49	0.91 (0.58–1.42)	0.680	1.14 (0.87–1.48)	0.347	1.09 (0.85–1.40)	0.501	0.86 (0.56–1.32)	0.490	1.02 (0.84–1.24)	0.835
rs4809958	209/240/54	211/219/68	0.79 (0.53–1.19)	0.261	1.10 (0.84–1.44)	0.474	1.03 (0.80–1.33)	0.829	0.75 (0.51–1.10)	0.146	0.95 (0.79–1.14)	0.582
rs56229249	296/186/20	275/179/36	0.51 (0.29–0.91)	**0.022**	0.96 (0.74–1.26)	0.781	0.89 (0.69–1.14)	0.354	0.52 (0.29–0.91)	**0.023**	0.84 (0.68–1.03)	0.099
rs2585428	168/252/83	151/254/93	0.80 (0.55–1.17)	0.252	0.89 (0.67–1.18)	0.407	0.87 (0.66–1.13)	0.290	0.87 (0.62–1.20)	0.390	0.90 (0.75–1.07)	0.234

Bold *p* values are significant. SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval. [a] Wild-type homozygote/heterozygote/variant homozygote.

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Table 4. Stratified analysis of *CYP24A1* polymorphisms and hypertension susceptibility

SNP	Model	Genotype	Men		Women		Age (≥61 years)		Age (<61 years)	
			OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
rs2762934	Allele	G	1.00		1.00		1.00		1.00	
		A	1.18 (0.82–1.69)	0.367	0.90 (0.56–1.43)	0.650	0.85 (0.58–1.24)	0.401	1.430.93–2.2)	0.099
	Codominant	GG	1.00		1.00		1.00		1.00	
		AG	1.33 (0.89–1.98)	0.166	1.24 (0.73–2.12)	0.429	0.97 (0.61–1.54)	0.904	1.96 (1.18–3.27)	**0.010**
		AA	0.55 (0.1–3.03)	0.489	–	–	–	–	0.40 (0.07–2.15)	0.283
	Dominant	GG	1.00		1.00		1.00		1.00	
		AA–AG	1.28 (0.86–1.89)	0.226	1.08 (0.64–1.82)	0.769	0.89 (0.57–1.41)	0.628	1.72 (1.06–2.82)	**0.029**
	Recessive	GG–AG	1.00		1.00		1.00		1.00	
		AA	0.52 (0.09–2.85)	0.447	–	–	–	–	0.35 (0.06–1.88)	0.221
	Additive		1.2 (0.83–1.72)	0.341	0.94 (0.59–1.51)	0.796	0.82 (0.54–1.27)	0.378	1.43 (0.92–2.21)	0.113
rs1977297	Allele	C	1.00		1.00		1.00		1.00	
		T	1.1 (0.86–1.4)	0.452	1.18 (0.88–1.59)	0.268	1.35 (1.05–1.73)	**0.018**	0.88 (0.66–1.19)	0.409
	Codominant	CC	1.00		1.00		1.00		1.00	
		CT	0.96 (0.68–1.34)	0.804	1.24 (0.81–1.9)	0.331	1.38 (0.95–2.01)	0.095	0.78 (0.51–1.19)	0.255
		TT	1.42 (0.77–2.62)	0.257	1.29 (0.68–2.45)	0.431	1.76 (0.93–3.34)	0.082	0.96 (0.48–1.91)	0.910
	Dominant	CC	1.00		1.00		1.00		1.00	
		TT–TC	1.02 (0.74–1.41)	0.904	1.25 (0.84–1.87)	0.276	1.44 (1.01–2.06)	**0.046**	0.81 (0.55–1.21)	0.314
	Recessive	CC–TC	1.00		1.00		1.00		1.00	
		TT	1.45 (0.81–2.61)	0.212	1.17 (0.64–2.14)	0.610	0.72 (0.40–1.31)	0.281	1.08 (0.56–2.08)	0.819
	Additive		1.09 (0.84–1.4)	0.519	1.17 (0.87–1.56)	0.302	1.35 (1.02–1.78)	**0.034**	0.90 (0.67–1.22)	0.513
rs2762940	Allele	A	1.00		1.00		1.00		1.00	
		C	1.28 (1.00–1.64)	0.051	0.76 (0.56–1.03)	0.076	1.04 (0.81––1.33)	0.764	1.03 (0.76–1.39)	0.860
	Codominant	AA	1.00		1.00		1.00		1.00	
		AC	1.42 (1.01–2.00)	**0.041**	0.81 (0.53–1.25)	0.343	1.30 (0.89–1.90)	0.168	0.98 (0.65–1.5)	0.939
		CC	1.34 (0.74–2.40)	0.333	0.53 (0.26–1.08)	0.079	0.82 (0.44–1.53)	0.525	1.19 (0.57–2.46)	0.646
	Dominant	AA	1.00		1.00		1.00		1.00	
		AC–CC	1.41 (1.02–1.95)	**0.038**	0.75 (0.50–1.12)	0.157	1.19 (0.83–1.71)	0.333	1.02 (0.68–1.51)	0.932
	Recessive	AA–AC	1.00		1.00		1.00		1.00	
		CC	1.13 (0.65–1.99)	0.662	0.60 (0.32–1.14)	0.120	0.63 (0.36–1.09)	0.098	1.2 (0.59–2.42)	0.622
	Additive		1.26 (0.98–1.62)	0.073	0.76 (0.56–1.03)	0.076	1.03 (0.79–1.35)	0.811	1.05 (0.77–1.42)	0.779
rs56229249	Allele	A	1.00		1.00		1.00		1.00	
		G	1.06 (0.81–1.38)	0.670	0.60 (0.43–0.83)	**0.002**	0.85 (0.65––1.11)	0.236	0.83 (0.6–1.15)	0.254
	Codominant	AA	1.00		1.00		1.00		1.00	
		GA	1.17 (0.83–1.64)	0.366	0.70 (0.46–1.08)	0.106	1.01 (0.69–1.46)	0.979	0.92 (0.6–1.41)	0.714
		GG	0.89 (0.42–1.89)	0.767	0.23 (0.09–0.59)	**0.003**	0.50 (0.22–1.16)	0.107	0.56 (0.23–1.36)	0.199
	Dominant	AA	1.00		1.00		1.00		1.00	
		GA–GG	1.13 (0.82–1.57)	0.456	0.60 (0.40–0.90)	**0.015**	0.93 (0.65–1.33)	0.672	0.86 (0.57–1.29)	0.463
	Recessive	AA–GA	1.00		1.00		1.00		1.00	
		GG	0.84 (0.40–1.76)	0.643	0.26 (0.10–0.67)	**0.005**	0.50 (0.22–1.14)	0.100	0.57 (0.24–1.38)	0.215
	Additive		1.07 (0.81–1.40)	0.652	0.59 (0.42–0.82)	**0.002**	0.86 (0.64–1.16)	0.326	0.83 (0.6–1.16)	0.280

Bold *p* values are significant. SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval.

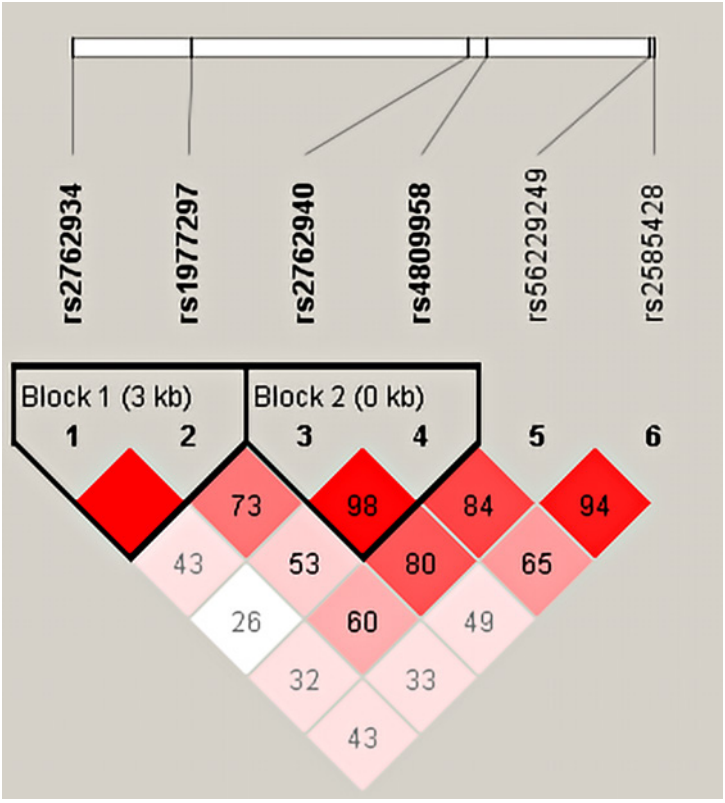

Fig. 1. Haplotype block map for the genetic variations of *CYP24A1.* Block 1 includes rs2762934 and rs1977297, block 2 includes rs2762940 and rs4809958. The LD between 2 SNPs is standardized D′.

showed a significant difference between *CYP24A1* rs2762934 and the low-density lipoprotein level (p = 0.036), and the level of UA was different in genotypes of *CYP24A1* rs2762940 (p = 0.030).

Discussion

The present study investigated 6 SNPs of *CYP24A1* and identified a significant association of 1 SNP (rs56229249) with the risk of hypertension. Specially, rs2762934 and rs1977297 significantly increased the hypertension risk in the subgroup of age. rs2762940 was associated with a higher hypertension risk in men and rs56229249 of *CYP24A1* had a protective function on hypertension in women. We also found two blocks (block 1: rs2762934 and rs1977297; block 2: rs2762940 and rs4809958).

CYP24A1 is an important cytochrome in P450 enzymes, mainly expressed in the kidney. The *CYP24A1* gene encodes the enzyme which plays a vital role in calcium homeostasis and the vitamin D endocrine system [20, 21]. Vitamin D, especially free vitamin D, is closely related to pathological conditions [22]. Disruption of *CYP24A1* in mice cause dysregulation of vitamin D metabolism [23]. The level of vitamin D has been reported as an important parameter for hypertension risk. To date, only a few studies have been conducted to assess associations between polymorphisms of the *CYP24A1* gene and hypertension susceptibility. Xiaoman et al. [24] evaluated the association between rs48009957, rs6068816 of *CYP24A1*, and hypertension risk in the Chinese Han population. It was reported in the Women's Genome Health Study that rs2296241 of *CYP24A1* showed associations with systolic BP, diastolic BP, mean arterial pressure, and pulse pressure [12]. Specifically, rs6013897 in the *CYP24A1* gene region

Table 5. Association between haplotypes of *CYP24A1* and hypertension susceptibility

SNP	Haplotype	Frequency in cases	Frequency in controls	OR (95% CI)	*p*
rs2762934|rs1977297	GT	0.332	0.305	1.12 (0.93–1.36)	0.239
rs2762934|rs1977297	AC	0.110	0.105	1.07 (0.80–1.43)	0.630
rs2762934|rs1977297	GC	0.442	0.410	1.14 (0.95–1.36)	0.158
rs2762940|rs4809958	AG	0.346	0.354	0.96 (0.80–1.15)	0.648
rs2762940|rs4809958	CT	0.303	0.293	1.03 (0.85–1.25)	0.759
rs2762940|rs4809958	AT	0.649	0.650	0.98 (0.81–1.17)	0.804

SNP, single nucleotide polymorphism; OR, odds ratio; CI, confidence interval.

had prominent significant associations with both systolic BP and diastolic BP [21]. In our study, a strong relationship between *CYP24A1* polymorphisms and hypertension risk was found, which might predict that genetic variants of *CYP24A1* significantly influence the susceptibility of hypertension.

Sex differences have been established in which men have a higher incidence of hypertension compared with women of the same age until the age of 60 years [25, 26]. Similarly, the increasing prevalence of hypertension with age has been demonstrated [27]. Hence, both can be regarded as genetic risks for hypertension. Then, when we further stratified by age and sex, we observed the strong relationships between genetic variants of *CYP24A1* and hypertension risk in our study. Among them, rs2762934 increased hypertension risk in codominant and dominant models for the subjects less than 61 years old, whereas rs1977297 was associated with higher hypertension risk in the subgroup of elderly individuals (≥61 years). This was consistent with previous studies and confirmed that hypertension risk is age dependent. In addition, rs2762940 is associated with a 1.42-fold risk of hypertension in men, while rs56229249 could be a protective factor for hypertension in women. The results may provide new possibilities for the individual treatment for hypertension. However, larger samples are required to validate the role of *CYP24A1* polymorphisms on hypertension susceptibility.

There are also some limitations to our study. First, all samples were recruited from a hospital, which inevitably introduced selection bias. Second, we did not analyze the influence of other risk factors, such as lifestyle, family history, and other lesions, because of the limited information. Third, we could not analyze the association of *CYP24A1* polymorphisms and more clinical factors because of the limited information we obtained from the study subjects. Hence, further experiments are needed to verify the associations between *CYP24A1* polymorphisms and hypertension risk.

Conclusion

The current findings show that polymorphisms of *CYP24A1* may represent important determinants of susceptibility to hypertension in the Chinese Han population and that their effects on disease risk are age and sex specific. Further functional studies and large, well-designed studies are expected to provide more evidence on how genetic variants of *CYP24A1* affect hypertension susceptibility.

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Statement of Ethics

Our study protocol was approved by the Affiliated Hospital of Inner Mongolia Medical University Ethics Committee, and written informed consent was obtained from all participants.

Disclosure Statement

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