Original Article

Association of the *ADIPOQ* Rs2241766 and Rs266729 Polymorphisms with Metabolic Syndrome in the Chinese Population: A Meta-analysis*

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Abstract

Objective This meta-analysis was performed to summarize the association of the *ADIPOQ* rs2241766 and rs266729 polymorphisms with metabolic syndrome (MS) in the Chinese population.

Methods We searched for articles in MEDLINE *via* PubMed, EMBASE, HuGE Navigator, CNKI, and Wanfang databases and calculated odds ratios (ORs) with 95% confidence intervals (CIs) to determine the strength of associations in fixed- or random-effects models.

Results We included 21 articles in the meta-analysis: 17 reports of *ADIPOQ* rs2241766 with 3628 cases and 3000 controls and 8 of rs266729 with 2021 cases and 2226 controls. We found an increased risk of MS with the *ADIPOQ* rs2241766 polymorphism in some genetic models (allele model: OR=1.12, 95% CI: 1.03-1.21; dominant model: OR=1.15, 95% CI: 1.04-1.28; homozygote model: OR=1.22, 95% CI: 1.00-1.49) but no association with the ADIPOQ rs266729 polymorphism (allele model: OR=0.98, 95% CI: 0.82-1.17; dominant model: OR=0.90, 95% CI: 0.79-1.02; recessive model: OR=1.09, 95% CI: 0.85-1.39; homozygote model: OR=1.03, 95% CI: 0.80-1.33).

Conclusion The results of this meta-analysis suggest an association between the *ADIPOQ* rs2241766 polymorphism and MS in the Chinese population. G allele of *ADIPOQ* rs2241766 increases the risk of MS. Better designed studies with different ethnic populations and larger sample sizes are needed for assessing the relationship between *ADIPOQ* rs2241766 and rs266729 polymorphisms and MS in the future.

Key words: *ADIPOQ*; Polymorphisms; Metabolic syndrome; Meta-analysis

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INTRODUCTION

Metabolic syndrome (MS) is a cluster of physiological and biochemical abnormalities, including abdominal obesity, dyslipidemia, hypertension and hyperglycemia[1]. Insulin resistance and central obesity are the core features of MS[1]. The prevalence of MS is increasing and is a public health problem worldwide. A previous study indicated that

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the adjusted prevalence of MS in middle-aged Chinese people in 2004-2005 had significantly increased since 1998 (10.0% *vs.* 7.2%, $P<0.05$)[2]. Data from the International Diabetes Federation (IDF) in 2005 showed that the prevalence of MS ranged from 10% to 50% among different populations with respect to ethnicity, nationality, sex, and age[3].

Previous studies suggested an association between hereditary factors and MS[4-5]. A large number of studies have reported MS-related candidate genes[6]. The adiponectin gene (*ADIPOQ*), located on chromosome 3q27, has been evaluated as a susceptibility locus for MS and its components[7-8]. Studies of a T/G mutation at position 45 in exon 2 and a C/G mutation at position -11377 in the promoter region in *ADIPOQ* were inconsistent. The +45T/G (rs2241766) sites were found closely related to obesity[9], type 2 diabetes[10], and MS[11]. However, other studies also found no significant association between rs2241766 polymorphism and obesity[12], MS[13], or hypertension[14]. A family-based study demonstrated that the *ADIPOQ* promoter variant rs266729 was associated with obesity and its traits in an Arabic population[15]. Other studies consistently revealed that the G allele of rs266729 might be a risk factor for type 2 diabetes[16-17]. However, Li et al.[11] found no significant association between the rs266729 polymorphism and MS.

Therefore, we conducted a meta-analysis to summarize the association between the *ADIPOQ* rs2241766 and rs266729 polymorphisms and MS in the Chinese population.

MATERIALS AND METHODS

Study Selection

We performed a systematic search of MEDLINE *via* PubMed, EMBASE, HuGE Navigator, CNKI, and Wanfang databases for articles evaluating the association between *ADIPOQ* polymorphisms and MS in the Chinese population published in English or Chinese. Moreover, we searched the reference lists and contacted the corresponding authors of all identified relevant publications. The search involved the following keyword strings: 'adiponectin', '*ADIPOQ*', 'adiponectin gene polymorphism', 'AMP1', 'metabolic syndrome', 'MS', 'metabolic syndrome X', 'syndrome X', 'genetic variability', 'allele', 'SNP', 'polymorphism', and 'Chinese'. All documents were updated to July 28, 2015.

Articles were included if they were a case-control or cross-sectional study published as an original study evaluating the association of the *ADIPOQ* rs2241766 and rs266729 polymorphisms with MS, if the outcome was MS defined by standard criteria, if the article provided sufficient data for evaluating odds ratios (ORs) with their 95% confidence intervals (95% CIs) directly or indirectly, and if control participants satisfied the Hardy-Weinberg equilibrium (HWE). The major exclusion criteria were articles in which genotype frequencies or alleles could not be ascertained, reviews or abstracts and studies which not studying on *ADIPOQ* polymorphisms or MS.

Data Extraction

Study selection and data extraction were conducted by two researchers (Zhou JM and Zhang M) independently. Data extracted included the author's last name, year of publication, ethnicity of subjects, study type, definition of MS, number of cases and controls, genotype frequencies in both groups and genotyping method, and the *P* value for HWE in control participants. Any disagreements were resolved by discussion or by consulting a third investigator (Hu DS).

Data Analysis

The association between *ADIPOQ* polymorphism and MS was estimated by ORs and 95% CIs in allele, dominant, recessive, and homozygote genetic models using Stata version 12.0 (STATA Corp., College Station, Texas, USA). A *Z* test was used to evaluate the statistical significance of the pooled ORs, with $P<0.05$ considered statistically significant. We used the inconsistency index I^2 to assess the heterogeneity of studies. Substantial heterogeneity was considered when $P_{het}<0.05$ or $I^2>50\%$, and the random-effects model was applied for assessing the pooled ORs and 95% CIs. The fixed-effects model was used in case of no substantial heterogeneity. We performed subgroup analyses by ethnicity; population region, divided as south and north by the Yangtze River; and criteria of MS defined by the Chinese Diabetes Society (CDS), IDF, Adult Treatment Panel III of the National Cholesterol Education Program (NCEP ATP III), World Health Organization (WHO), or De Ferranti et al.[18]. Sensitivity analysis, conducted by removing one study at a time and calculating the pooled ORs for the remaining studies, was performed to assess the stability of the results. We used Egger's test (reported as *t* and *P* values) to estimate

publication bias. $P<0.05$ was considered statistically significant.

Quality Score Assessment for the Included Studies

The quality of the included studies was assessed using the Ottawa-Newcastle system (NOS)[19]. The NOS uses a star rating system to judge quality based on three broad perspectives: selection of study groups, comparability of categories, and ascertainment of exposure. A maximum of one star is given for each numbered item within the selection and exposure categories. A maximum of two stars is given for comparability. Studies with a total score ≥7 were considered high quality.

RESULTS

Characteristics of Studies

Our literature search yielded 112 articles identified by searching databases and an additional 10 articles identified by searching the reference lists and contacting the corresponding authors of all identified related publications (Figure 1). We preliminarily included 22 articles[13,20-40] and tested genotype frequencies for HWE in control participants to confirm eligibility. For studies evaluating the rs2241766 polymorphism and MS, with α=0.003 (0.05/18≈0.003) used to measure HWE, controls deviated from HWE in one paper[40]. We included 17 publications for the association between rs2241766 polymorphism and MS (Table 1, Figure 1). For studies evaluating the association between rs266729 polymorphism and MS, with α=0.006 (0.05/8≈0.006) used to test HWE, all control groups satisfied HWE. Finally, we included only 8 articles on the association between rs266729 polymorphism and MS (Table 1, Figure 1). Four articles described both polymorphisms. Most studies had a case-control design. The median quality score for included studies was 6.95 (range 6-8); 71.4% were considered a relatively high quality.

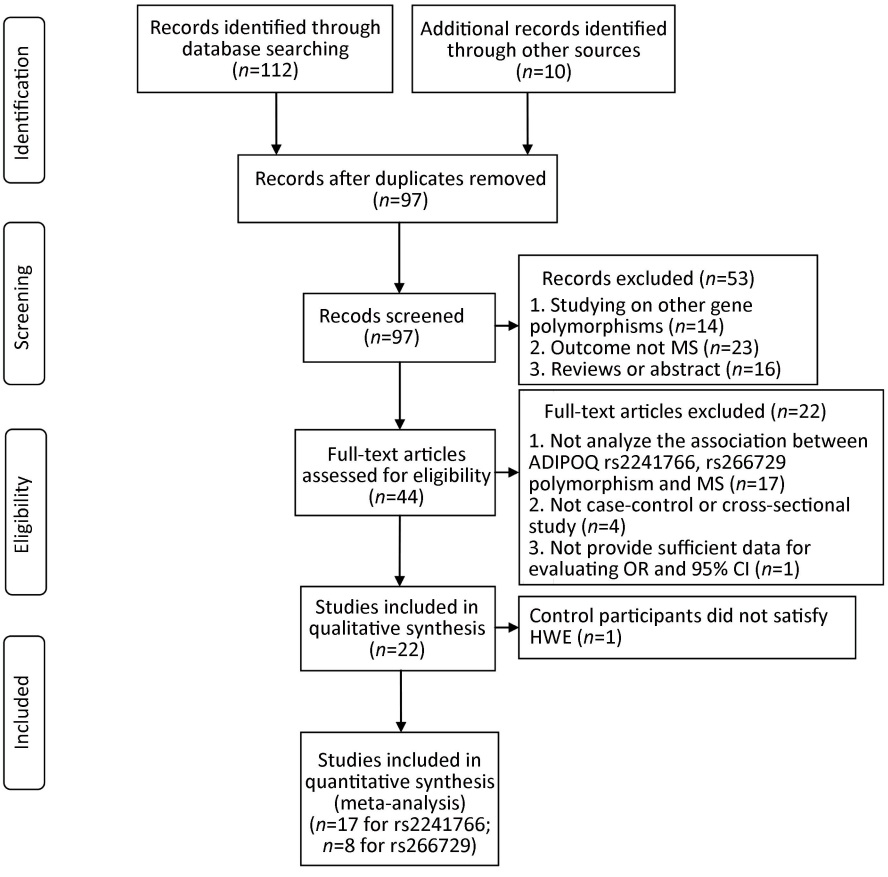

Figure 1. Flow diagram of included studies.

Table 1. Characteristics of the Studies Included in the Meta-analysis

SNPs and Author (year)	Ethnicity	Study Type	MS Definition	Genotyping Method	Sample Size*		Genotype Frequency in Cases#			Genotype Frequency in Controls#			P_{HWE}	NOS Scores
					Cases	Controls	TT / CC	TG / CG	GG	TT / CC	TG / CG	GG		
rs2241766 (T/G)														
Bu RF (2011)[20]	Han Chinese	case-control	CDS	TaqMan	195	156	76	97	22	79	67	10	0.40	8
Cai Q (2010)[21]	Chinese	case-control	IDF	PCR-RFLP	38	50	15	18	5	26	20	4	0.96	6
Chen F (2011)[22]	Chinese	case-control	CDS	PCR-RFLP	136	102	63	58	15	59	35	8	0.39	8
Chen F (2012)[23]	Han Chinese	case-control	CDS	PCR-RFLP	107	102	53	49	5	59	35	8	0.39	7
Gao M (2013)[24]	Han Chinese	case-control	IDF	PCR-RFLP	322	161	147	158	17	93	61	7	0.44	7
Leu HB (2011)[25]	Taiwanese	case-control	NCEP ATPIII	TaqMan	357	605	170	156	31	307	251	47	0.66	7
Huang FZ (2014)[26]	Han Chinese	case-control	IDF	PCR-RFLP	448	400	235	184	29	215	160	25	0.51	6
Li P (2012)[35]	Chinese	case-control	IDF	PCR-RFLP	47	367	26	15	6	212	138	17	0.36	7
Li XT (2012)[27]	Han Chinese	case-control	CDS	PCR-RFLP	116	108	71	40	5	76	28	4	0.49	8
Li YP (2008)[30]	Han Chinese	case-control	IDF	PCR-RFLP	64	40	24	34	6	10	26	4	0.04	6
Li YP (2009)[29]	Han Chinese	case-control	IDF	PCR-RFLP	88	56	38	41	9	23	26	7	0.93	6
Li YP (2010)[28]	Chinese	case-control	IDF	PCR-RFLP	137	131	69	54	14	56	60	15	0.86	6
Liu DX (2006)[31]	Chinese	cross-sectional	IDF	TaqMan	156	133	73	66	17	69	53	11	0.85	7
Wang SJ (2012)[13]	Han Chinese	case-control	WHO	PCR-RFLP	344	50	188	135	21	31	16	3	0.63	7
Xu J (2013)[32]	Han Chinese	cross-sectional	IDF	TaqMan	701	206	368	274	59	97	93	16	0.33	7
Yao M (2004)[33]	Chinese	case-control	WHO	PCR-RFLP	189	189	91	79	18	87	77	22	0.44	8
Zhu XW (2010)[34]	Han Chinese	case-control	CDS	TaqMan	183	144	72	91	20	74	62	8	0.28	7
Rs266729 (C/G)														
Lin CH (2012)[36]	Taiwanese	case-control	Modified NCEP ATP III	PCR-RFLP	137	110	77	50	10	64	40	6	0.94	7
Gao M (2013)[24]	Han Chinese	case-control	IDF	PCR-RFLP	322	161	188	103	9	85	65	6	0.13	7
Du J (2012)[37]	Han Chinese	case-control	IDF	TaqMan	992	1022	555	353	84	530	410	82	0.83	7
Li P (2012)[35]	Chinese	case-control	IDF	PCR-RFLP	47	367	22	24	1	179	146	42	0.15	7
Li YP (2009)[29]	Han Chinese	case-control	IDF	PCR-RFLP	88	56	50	33	5	26	25	5	0.77	6
Li YP (2010)[28]	Chinese	case-control	IDF	PCR-RFLP	137	131	78	48	11	63	60	8	0.20	6
Wang LJ (2013)[38]	Han Chinese	cross-sectional	CDS	PCR-RFLP	150	150	87	46	17	94	48	8	0.57	6
Ye P (2013)[39]	Chinese	case-control	De Ferranti	PCR-RFLP	114	114	66	41	7	81	28	3	0.76	8

Note. CDS: Chinese Diabetes Society; IDF: International Diabetes Federation; NCEP ATP III: Adult Treatment Panel III of the National Cholesterol Education Program; WHO: World Health Organization; P_{HWE}: *P* value for Hardy-Weinberg equilibrium in control participants; NOS scores: The scores of the included studies assessed by the Ottawa-Newcastle system. *The numbers of case or control group included in the original study; #The data of genotype frequency in case or control group were used to analyze the association between gene loci and MS.

Association between rs2241766 and MS

For the association between rs2241766 and MS, 3628 cases and 3000 controls were identified. Figure 2 shows the forest plots of MS risk associated with the *ADIPOQ* rs2241766 polymorphism in the allele (A), dominant (B), recessive (C), and homozygote (D) models. The fixed-effects model generated a combined allelic OR of 1.12 (95% CI: 1.03-1.21, *P*=0.006) for the G allele, 1.15 (95% CI: 1.04-1.28, *P*=0.008) for the TG+GG genotype in the dominant model, 1.17 (95% CI: 0.96-1.42, *P*=0.114) for the GG genotype in the recessive model, and 1.22 (95% CI: 1.00-1.49, *P*=0.047) for the GG genotype in the homozygote model (Figure 2, Table 2), for a significant association between the *ADIPOQ* rs2241766 polymorphism and overall risk of MS except in the recessive model.

Regarding ethnicity, MS risk was increased with the rs2241766 polymorphism in three of the genetic models, the allele model (OR=1.18, 95% CI: 1.05-1.34), dominant model (OR=1.22, 95% CI: 1.04-1.43), and homozygote model (OR=1.40, 95% CI: 1.05-1.88) in all Chinese (not just Han Chinese) but not in Han Chinese alone. MS risk was increased with the rs2241766 polymorphism in the allele model in both the north (OR=1.17, 95% CI: 1.04-1.31) and south (OR=1.13, 95% CI: 1.00-1.29) regions, but in the dominant model only in the north (OR=1.24, 95% CI: 1.07-1.44). Regarding MS definition, MS risk was increased only with the CDS diagnostic criteria in the allele (OR=1.40, 95% CI: 1.18-1.66), and dominant (OR=1.56, 95% CI: 1.25-1.94) models (Table 2).

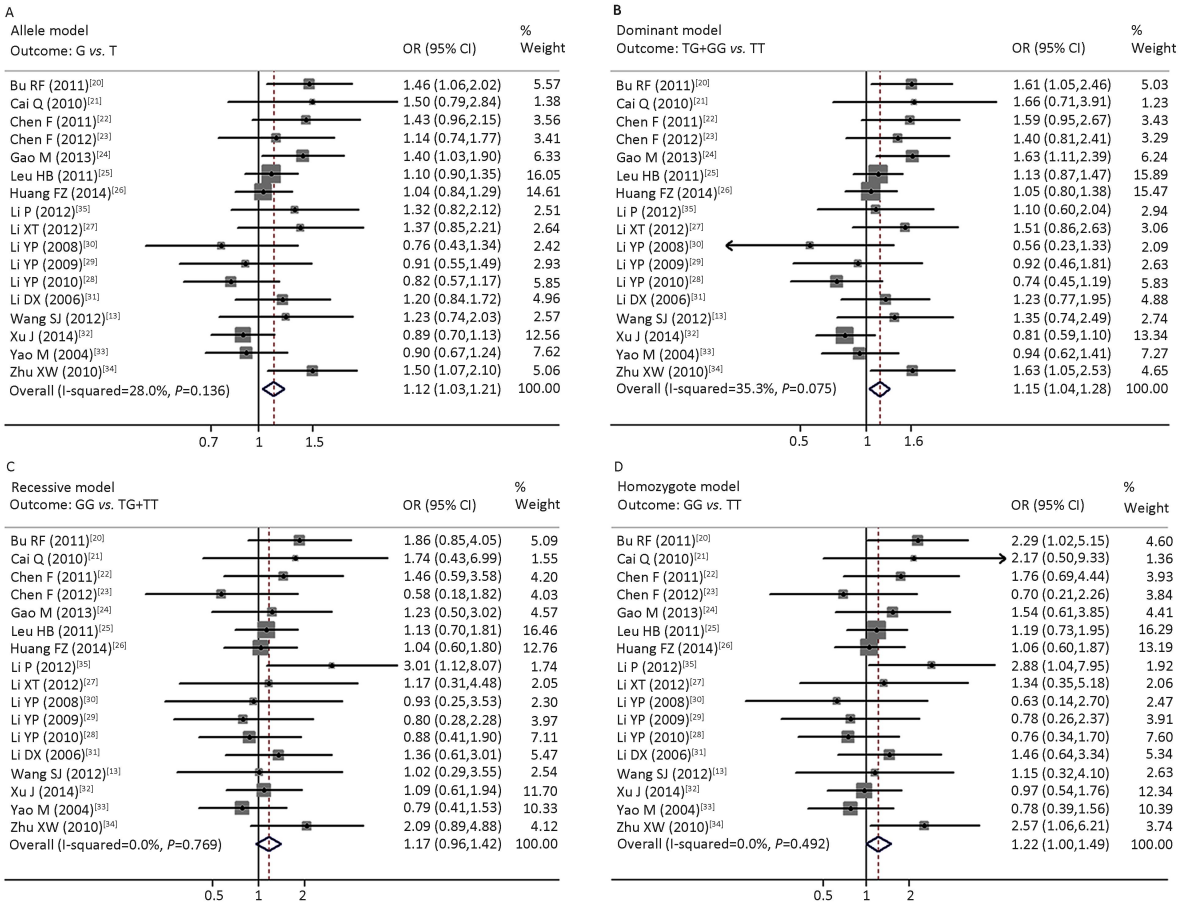

Figure 2. Forest plots of the risk of MS associated with the *ADIPOQ* rs2241766 polymorphism in the allele (A), dominant (B), recessive (C), and homozygote (D) models. The squares and horizontal lines correspond to the study-specific odds ratios (ORs) and 95% confidence intervals (CIs). The area of each square reflects the study-specific weight. The diamonds represent the combined ORs with its 95% CIs.

Table 2. Subgroup Analyses of Associations between the *ADIOPQ* Polymorphisms and MS by Genetic Model

Variable	*N*	Allele Model			Dominant Model			Recessive Model			Homozygote Model		
		OR (95% CI)	P_{het}	I^2 (%)	OR (95% CI)	P_{het}	I^2 (%)	OR (95% CI)	P_{het}	I^2 (%)	OR (95% CI)	P_{het}	I^2 (%)
rs2241766													
Overall	17	1.12 (1.03, 1.21)	0.136	28.0	1.15 (1.04, 1.28)	0.075	35.3	1.17 (0.96, 1.42)	0.769	0.0	1.22 (1.00, 1.49)	0.492	0.0
Ethnicity													
Han Chinese	10	1.08 (0.97, 1.20)	0.115	36.7	1.11 (0.97, 1.27)	0.028	51.9	1.07 (0.82, 1.39)	0.927	0.0	1.09 (0.83, 1.43)	0.717	0.0
Chinese	7	1.18 (1.05, 1.34)	0.352	10.1	1.22 (1.04, 1.43)	0.519	0.0	1.29 (0.98, 1.72)	0.342	11.4	1.40 (1.05, 1.88)	0.277	0.0
Region[a]													
South	7	1.13 (1.00, 1.29)	0.086	45.8	1.16 (0.99, 1.37)	0.077	47.4	1.22 (0.91, 1.64)	0.636	0.0	1.28 (0.95, 1.74)	0.255	22.8
North	9	1.17 (1.04, 1.31)	0.520	0.0	1.24 (1.07, 1.44)	0.503	0.0	1.14 (0.86, 1.51)	0.510	0.0	1.24 (0.93, 1.66)	0.531	0.0
Definition of MS													
CDS	5	1.40 (1.18, 1.66)	0.895	0.0	1.56 (1.25, 1.94)	0.994	0.0	1.48 (0.98, 2.24)	0.456	0.0	1.79 (1.16, 2.74)	0.456	0.0
IDF	9	1.04 (0.93, 1.17)	0.195	28.1	1.03 (0.89, 1.19)	0.092	41.3	1.14 (0.87, 1.50)	0.715	0.0	1.13 (0.85, 1.50)	0.525	0.0
Others[b]	3	1.06 (0.90, 1.24)	0.507	0.0	1.10 (0.90, 1.35)	0.578	0.0	1.00 (0.69, 1.44)	0.688	0.0	1.04 (0.71, 1.53)	0.614	0.0
Rs266729													
Overall	8	0.98 (0.82, 1.17)	0.048	50.6	0.90 (0.79, 1.02)	0.071	46.4	1.09 (0.85, 1.39)	0.264	20.8	1.03 (0.80, 1.33)	0.199	28.7
Ethnicity													
Han Chinese	4	0.92 (0.74, 1.14)	0.117	49.2	0.85 (0.73, 0.98)	0.307	16.9	1.10 (0.83, 1.45)	0.264	23.3	1.02 (0.77, 1.36)	0.186	37.7
Chinese	4	1.07 (0.77, 1.49)	0.073	56.9	1.08 (0.83, 1.41)	0.070	57.5	1.04 (0.60, 1.78)	0.165	41.1	1.07 (0.61, 1.87)	0.182	38.4
Region													
South	6	1.05 (0.84, 1.31)	0.033	58.7	0.92 (0.80, 1.05)	0.046	55.8	1.19 (0.92, 1.55)	0.452	0.0	1.12 (0.86, 1.46)	0.274	21.2
North	2	0.79 (0.60, 1.04)	0.778	0.0	0.81 (0.58, 1.12)	0.259	21.4	0.44 (0.19, 1.05)	0.159	49.5	0.44 (0.18, 1.08)	0.261	20.7
Definition of MS													
IDF	5	0.87 (0.78, 0.98)	0.811	0.0	0.82 (0.71, 0.94)	0.692	0.0	0.96 (0.73, 1.26)	0.355	9.0	0.88 (0.66, 1.17)	0.465	0.0
Others[c]	3	1.35 (1.06, 1.72)	0.339	7.5	1.32 (0.99, 1.77)	0.309	14.8	1.94 (1.07, 3.54)	0.725	0.0	2.04 (1.11, 3.75)	0.669	0.0

Note. *N*: number of the articles; [a]: Xu et al. didn't state clear area where people came from; [b]: NCEP ATP III, WHO; [c]: NCEP ATP III, CDS: De Ferranti.

Association between rs266729 and MS

In total, 2021 MS patients and 2226 controls were analyzed for the association between rs266729 and MS. Figure 3 depicts forest plots of MS risk with *ADIPOQ* rs266729 polymorphism in the allele (A), dominant (B), recessive (C), and homozygote (D) models. The allele model presented significant heterogeneity (I^2=50.6%, P_{het}=0.048). Thus, the random-effects model was used to generate a combined allelic OR of 0.98 (95% CI: 0.82-1.17, *P*=0.802) for the G allele. We obtained a combined OR of 0.90 (95% CI: 0.79-1.02, *P*=0.104) for the CG+GG genotype in the dominant model, 1.09 (95% CI: 0.85-1.39, *P*=0.508) for the GG genotype in the recessive model, and 1.03 (95% CI: 0.80-1.33, *P*=0.816) for the GG genotype in the homozygote model using the fixed-effects model (Figure 3; Table 2). All these genetic models displayed no association between rs266729 polymorphism and MS in the overall analyses.

Regarding the MS definition, MS risk was increased with the CDS, NCEP ATP III, and De Ferranti definitions, but not with the IDF definition, in the allele (OR=1.35, 95% CI: 1.06-1.72), recessive (OR=1.94, 95% CI: 1.07-3.54), and homozygote (OR=2.04, 95% CI: 1.11-3.75) models. MS risk was not associated with the rs266729 polymorphism according to ethnicity or region in any model (Table 2).

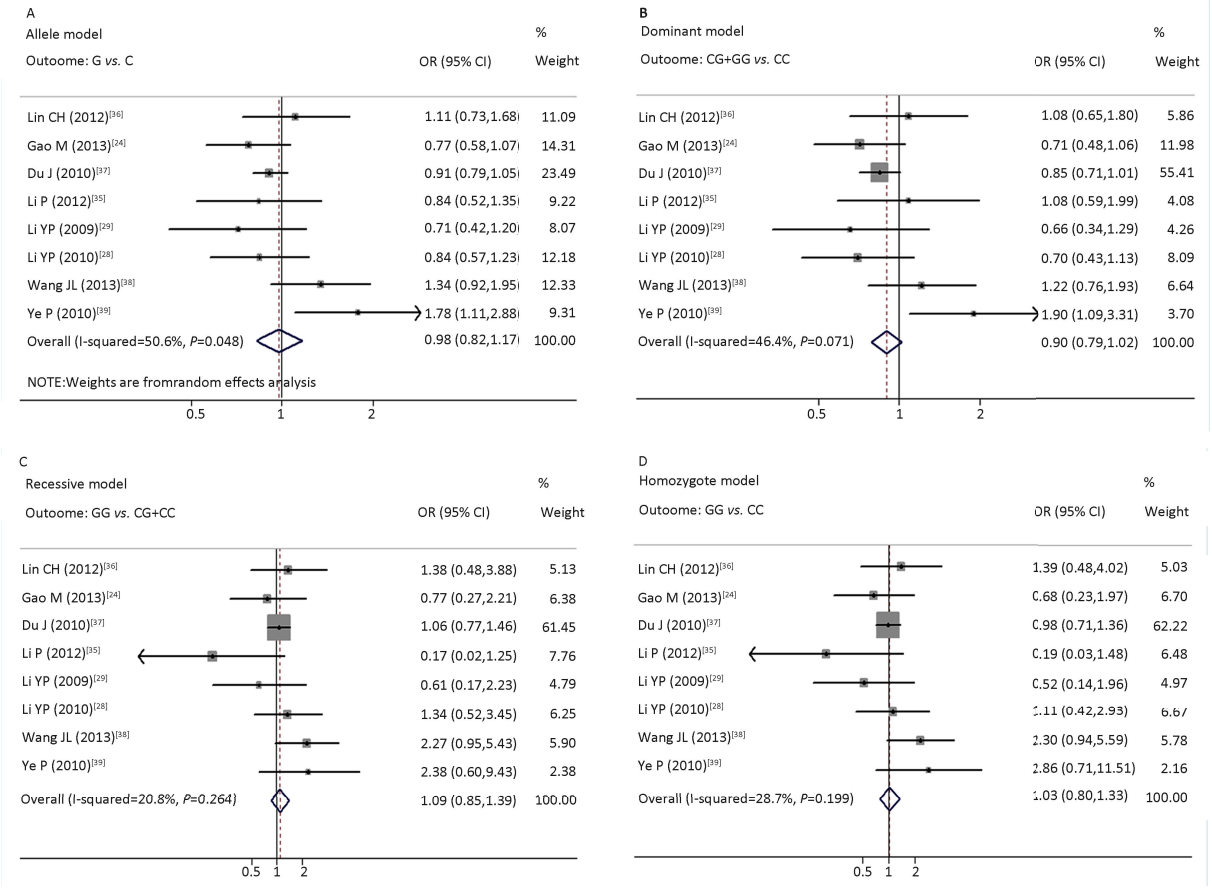

Figure 3. Forest plots of risk of MS associated with *ADIPOQ* rs266729 polymorphism in allele (A), dominant (B), recessive (C), homozygote (D) models. The squares and horizontal lines correspond to the study-specific ORs and 95% CIs. The area of each square reflects the study-specific weight. The diamonds represent the combined ORs with its 95% CIs.

Heterogeneity Analysis

For the rs2241766 polymorphism, we found no significant heterogeneity among studies in the overall analyses (allele model: I^2=28.0%, P_{het}=0.136; dominant model: I^2=35.3%, P_{het}=0.075; recessive model: I^2=0.0%, P_{het}=0.769; and homozygote model: I^2=0.0%, P_{het}=0.492) (Table 2). For the rs266729 polymorphism, the allele model showed substantial heterogeneity among studies (I^2=50.6%, P_{het}=0.048), with no evidence of heterogeneity for other models (dominant model: I^2=46.4%, P_{het}=0.071; recessive model: I^2=20.8%, P_{het}=0.264; and homozygote model: I^2=28.7%, P_{het}=0.199) (Table 2).

Sensitivity Analysis and Publication Bias

The sensitivity analysis showed that no individual study affected the overall conclusions. Therefore, our meta-analysis results were stable and reliable. Moreover, we found no publication bias according to the Egger's test (Table 3).

DISCUSSION

In this meta-analysis of the association of *ADIPOQ* rs2241766 and rs266729 with MS in the Chinese population, MS risk was increased with the rs2241766 polymorphism in the allele, dominant and homozygote models, but the rs266729 polymorphism was not associated with MS in any model. This meta-analysis suggested an association between the *ADIPOQ* rs2241766 polymorphism and MS in the Chinese population. G allele of *ADIPOQ* rs2241766 increased the risk of MS.

Adiponectin, a specific protein produced by fat cells, functions as a collagen-like protein hormone with anti-diabetic, anti-inflammatory, anti-atherosclerotic[11] and insulin-sensitizing properties[41]. A meta-analysis of genome-wide association analyses indicated that the *ADIPOQ* was the only major gene for plasma adiponectin, which explained 6.7% of the phenotypic variance[42]. A previous study showed that synonymous mutation of *ADIPOQ* locus may affect steady-state mRNA levels by altering RNA splicing or stability[43], suggesting an allele-specific differential expression of adiponectin. Alterations of plasma adiponectin levels due to such differential expression of adiponectin have been linked to MS and its components[44]. A variant of *ADIPOQ* rs2241766 G/T was reported to be related to low serum levels of adiponectin[45-47]. The *ADIPOQ* exon 45 G allele point mutation was discovered as a risk factor for type 2 diabetes mellitus in both Chinese[48] and Japanese populations[49]. The *ADIPOQ* rs266729 polymorphism has been shown to affect circulating adiponectin concentrations and significantly increase the risk of MS among people in Thailand[50] and Croatia[51].

In the current study, we found the rs2241766 variant was significantly associated with MS, which is consistent with another systematic meta-analysis including 2684 cases and 2864 controls in a Chinese population[24]. In contrast, no relationship was found between SNP+45T>G and MS among Asian Indians[52] or Malaysians[53]. We found the rs2241766 polymorphism associated with MS in all Chinese (not just Han Chinese) but not in Han Chinese alone. The inconsistent results among the publications might be due to the different genetic backgrounds of the study populations. The strength of the association between the rs2241766 polymorphism and MS differed by region in China. One reason could be that the link between genetic variation and disease can be modified by different dietary patterns[54-55]. Populations from different geographical regions might have different lifestyles and dietary patterns, which might influence the genetic variant affecting MS. In addition, Yao et al.[56] found that the genetic

Table 3. Results of Egger's Test for Publication Bias

SNP	Comparison	No. of Studies	*t*	*P* Value
rs2241766	G *vs.* T (allele)	17	0.91	0.375
	(TG+GG) *vs.* TT (dominant)	17	0.60	0.556
	GG *vs.* (TG+TT) (recessive)	17	0.55	0.59
	GG *vs.* TT (homozygote)	17	0.66	0.518
rs266729	G *vs.* C (allele)	8	0.63	0.551
	(CG+GG) *vs.* CC (dominant)	8	0.86	0.425
	GG *vs.* (CG+CC) (recessive)	8	0.20	0.845
	GG *vs.* CC (homozygote)	8	0.04	0.969

backgrounds of populations from the south and north of China differed, which might also affect the role of the gene variants in MS.

Our meta-analysis of 2021 cases and 2226 controls showed that rs266729 was not associated with MS in all genetic models in the overall analysis. However, another meta-analysis conducted by Li et al.[57] stated that rs266729 was significantly associated with type 2 diabetes mellitus in the Chinese population. The reason for the inconsistent results of above-mentioned two studies was that MS and type 2 diabetes mellitus are different metabolic status[58] and they have different diagnostic criteria although a highly proportion of type 2 diabetes mellitus patients could have MS[59]. Some studies demonstrated that the genetic variation associated with type 2 diabetes mellitus may not be related to MS[59-60], and it seems that the genetic variation associated with MS might be related to type 2 diabetes mellitus with higher possibility[61]. Subgroup analysis by definition of MS demonstrated that rs266729 could contribute to MS risk using definitions other than the IDF definition, so the definition of MS could affect the results of an analysis of a relationship between the rs266729 polymorphism and MS. MS does not have an optimal definition, and different criteria may lead to discordant results[62-63]. Each set of diagnostic criteria of MS has its own characteristics, and the IDF criteria are more conservative than other criteria for diagnosing MS, which leads to inconsistent results[64]. We could have performed subgroup analysis based on sample size, but the total sample size of the five included studies in our study was <400[28-29,36,38-39], which limited the quality of stratified statistical results.

Our study contains some limitations. First, we did not analyze the effects of gene-gene and gene-environment interactions because of a lack of relevant information, although MS has been reported to result from the interactions of genetic factors and environmental factors such as dietary factors[65-66]. Second, our study was limited to papers published in English and Chinese. Third, our analyses were based primarily on unadjusted effect estimates without controlling for confounding factors because of a lack of original data.

In conclusion, this meta-analysis showed that the *ADIPOQ* rs2241766 polymorphism was associated with a risk of MS in the Chinese population but failed to reveal any association for the *ADIPOQ* rs266729 polymorphism in the overall analysis. Further investigations including additional original research with different ethnic populations should be conducted.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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