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