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Meta-Analyse

The association between paraoxonase 1 gene polymorphisms and polycystic ovarian syndrome

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Abstract: Some studies investigated the association of paraoxonase 1 (PON1) polymorphisms with polycystic ovarian syndrome (PCOS) risk. However, the result was still inconsistent. The aim of this study was to investigate whether there is an association between the PON1 polymorphisms and PCOS risk. Electronic databases, such as PubMed, EMBASE, and China National Knowledge Infrastructure (CNKI) databases, were searched for identification of the studies. The associations between PON1 polymorphisms and PCOS risk was quantified using ORs with 95% CIs. A total of 8 eligible studies with 2272 cases and 1811 controls were included in this meta-analysis. PON1 Leu55Met polymorphism was associated with a significantly increased risk of PCOS (OR=1.31; 95%CI, 1.10-1.55). However, no association was found in Asians and Caucasians (Table 2). We also found that PON1 Q192R polymorphism was associated with a significantly increased risk of PCOS (OR=1.81; 95%CI, 1.17-2.82). Additionally, this polymorphism increased PCOS risk in Asians (OR=1.26; 95%CI, 1.13-1.41). Furthermore, PON1 C108T polymorphism showed increased PCOS risk (OR=1.46; 95%CI, 1.08-1.97). No association between this polymorphism and PCOS risk was found in Asians and Caucasians. In conclusion, this meta-analysis suggested that PON1 polymorphisms were associated with PCOS risk.

Key words: Polycystic ovarian syndrome, paraoxonase 1, risk.

Introduction

Polycystic ovarian syndrome (PCOS) is one of the most common endocrine disorders affecting 5–10% of women of reproductive age (1). PCOS is defined when PCOS patients belong to two of the three criteria: oligo- or anovulation, hyperandrogenism, and polycystic ovaries (2). The pathogenesis and mechanism of PCOS remain unclear. Genetic factors are supposed to play an important role in the development of PCOS.

Paraoxonase 1 (PON1) has been most intensely studied in relation to the risk of cardiovascular disease, stroke, oxidative stress and inflammation. It was first studied for its organophosphatase activity which explained its ability to detoxify organophosphate through hydrolysis and thus provide neuroprotection against the effects of environmental neurotoxins and age-related neurodegeneration (3). Human serum PON1 levels and activity display an up to 40-fold interindividual variability and are genetically associated with a single nucleotide polymorphism (SNP) in the PON1 gene. Some studies investigated the association of PON1 polymorphisms with PCOS risk (4-11). However, the result was still inconsistent. The aim of this study was to investigate whether there is an association between the PON1 polymorphisms and PCOS risk.

Materials and Methods

Search strategies

Electronic databases, such as PubMed, EMBASE, and China National Knowledge Infrastructure (CNKI) databases, were searched for identification of the studies. The last search was up to July 10, 2016. Search terms included “Polycystic ovarian syndrome or PCOS” and “Paraoxonase 1 or PON1”. All searched studies were retrieved and the bibliographies were checked for other relevant publications.

Inclusion criteria

The following criteria were used to select the eligible studies: (a) evaluation of the association between PON1 polymorphisms and PCOS risk; (b) an unrelated case–control study in which family members were excluded; (c) sufficient published data for estimating an odds ratio (OR) with 95% confidence interval (CI). When authors reported two or more publications on the same patient population, only the largest study was selected. Additionally, when a study reported the results on different subpopulations, we treated them as a separate study.

Data extraction

Data were extracted by two authors independently. The following information was extracted from each study: first author, year of publication, ethnicity, age, body mass index, sample size, and Hardy-Weinberg equilibrium (HWE) results.

Statistical analysis

The associations between PON1 polymorphisms and PCOS risk was quantified using ORs with 95% CIs. The pooled ORs and 95% CIs were estimated by allelic models. A statistical test for heterogeneity was performed based on the Q statistic. The P>0.10 of the Q-test indicated a lack of heterogeneity among studies. The summary OR estimate of each study was calculated by

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Table 1. Characteristics of the included studies.

First author	Year	Ethnicity	Age (y)	BMI (kg/m^2)	Case (n)	Control (n)	Polymorphism	HWE
Lenarcik	2010	Caucasian	25	27	130	70	Leu55Met	Yes
Wang	2012	Asian	24	22	610	503	Leu55Met, Q192R	Yes
Paltoglou	2013	Caucasian	25	27	142	112	Leu55Met, Q192R, C108T	Yes
Ferk	2014	Caucasian	24	22	118	108	C108T	Yes
Woo	2014	Asian	25	21	196	166	C108T	Yes
Dadachanji	2015	Asian	24	NA	482	326	Leu55Met, Q192R	Yes
Zhang	2015	Asian	25	23	455	441	Leu55Met, Q192R, C108T	Yes
Millán	2016	Caucasian	25	NA	139	85	C108T	Yes

BMI, body mass index; HWE, Hardy-Weinberg equilibrium; NA, not available.

the random-effects model (the DerSimonian and Laird method). Stratified analysis was performed by race. All statistical tests were performed with the Revman 5.1 software (Nordic Cochrane Center, Copenhagen, Denmark). A P value <0.05 was considered statistically significant.

Results

Study characteristics

In this current study, a total of 8 eligible studies met the inclusion criteria. Finally, a total of 2272 cases and 1811 controls were included in this meta-analysis. There were 4 studies performed using Asians and 4 studies using Caucasians. Three polymorphisms, such as Leu55Met, Q192R, and C108T, were investigated in this meta-analysis. Characteristics of studies are presented in Table 1.

Meta-analyses results

The results of meta-analysis are presented in Table 2. PON1 Leu55Met polymorphism was associated with a significantly increased risk of PCOS (OR=1.31; 95%CI, 1.10-1.55; Figure 1). However, no association was found in Asians and Caucasians (Table 2). We also found that PON1 Q192R polymorphism was associated with a significantly increased risk of PCOS (OR=1.81; 95%CI, 1.17-2.82; Figure 2). Additionally, this polymorphism increased PCOS risk in Asians (OR=1.26; 95%CI, 1.13-1.41). Furthermore, PON1 C108T polymorphism showed increased PCOS risk (OR=1.46; 95%CI, 1.08-1.97; Figure 3). No association between this polymorphism and PCOS risk was found in Asians and Caucasians (Table 2).

Table 2. Results of meta-analysis.

Polymorphism	OR (95% CI)	*P* Value	I^2 (%)
Leu55Met	1.31 (1.10-1.55)	0.002	33
Asian	1.21 (0.97-1.49)	0.09	0
Caucasian	1.46 (0.91-2.34)	0.12	66
Q192R	1.81 (1.17-2.82)	0.008	93
Asian	1.26 (1.13-1.41)	<0.0001	0
C108T	1.46 (1.08-1.97)	0.01	71
Asian	1.34 (0.83-2.16)	0.23	65
Caucasian	1.58 (0.97-2.57)	0.06	77

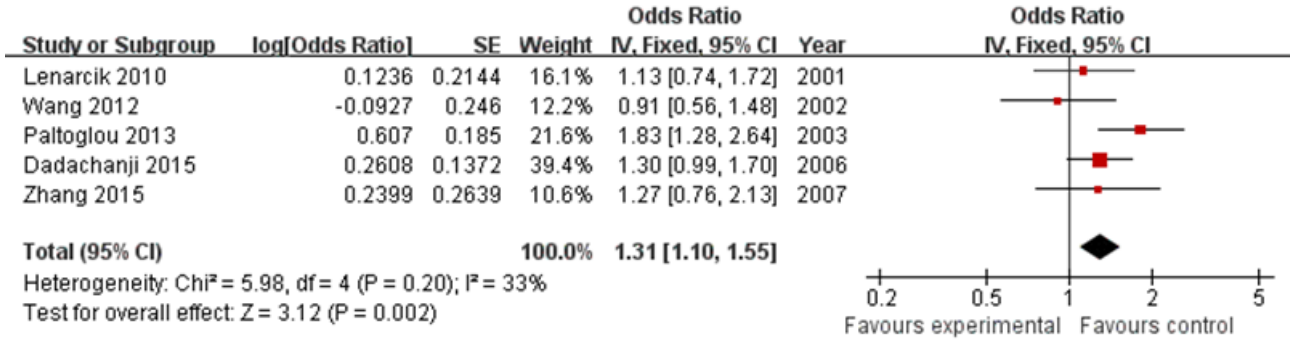

Figure 1. The forest plot of PON1 Leu55Met polymorphism and PCOS risk.

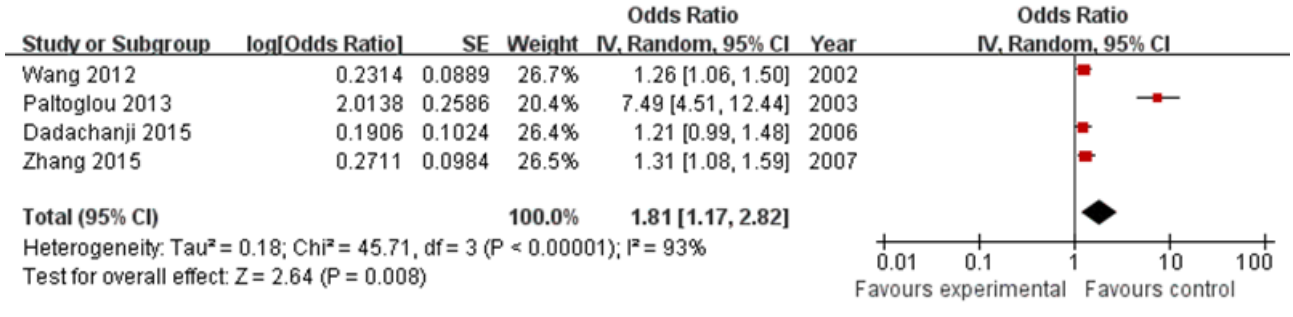

Figure 2. The forest plot of PON1Q192R polymorphism and PCOS risk.

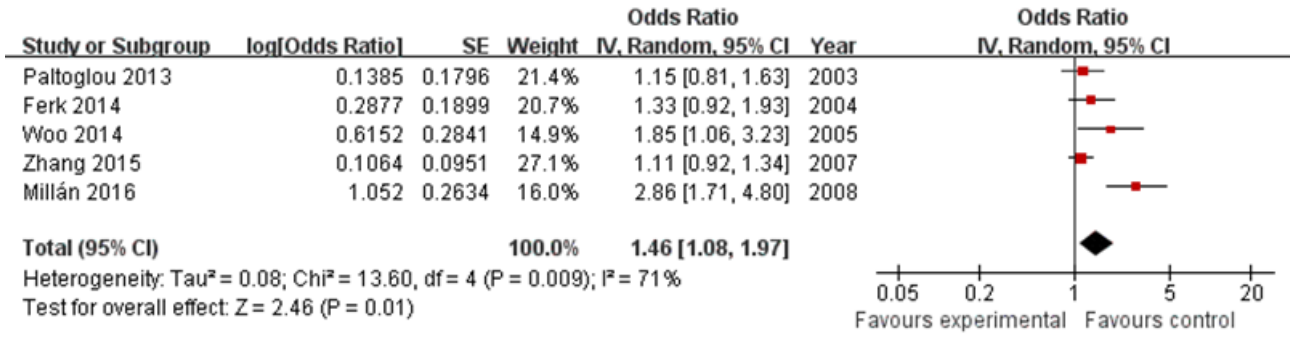

Figure 3. The forest plot of PON1 C108T polymorphism and PCOS risk.

Discussion

To the best of our knowledge, this is the first meta-analysis of the association between PON1 polymorphisms and PCOS risk. PON1 Leu55Met, Q192R, and C108T polymorphisms were associated with a significantly increased risk of PCOS. However, no association between Leu55Met and C108T polymorphisms was found in Asians and Caucasians. Additionally, PON1 Q192R polymorphism increased PCOS risk in Asians.

Baskol et al. suggested that PON1 activity was lower in women with PCOS than in the control women (12). Soyman et al. also found that Serum PON1 activity was statistically significantly lower in women with PCOS compared with healthy controls matched for age and BMI (13). Dursun et al. indicated that deduced serum PON1 activity might contribute to the increased susceptibility for the development of atherosclerotic heart disease in women with PCOS (14).

Baig et al. suggested that PON1 Q192R polymorphism is likely to be a risk factor for cataract development in Pakistani population while PON1 L55M was not found to be associated with cataract (15). Chen et al. indicated that PON1-L55M allele increased the risk of cancer (16). Fekih et al. demonstrated that PON1 polymorphisms L55M and Q192R seem to be a genetic marker involved in the development of diabetic nephropathy in diabetes (17).

There are several limitations in this study. First, only 8 studies were included in this study. Consequently, this study maybe lack of power due to the small number of studies. Second, due to the lack of original information of the entire data, we did not evaluate interactions of gene and environmental factors in all pooled studies. Third, we only included published English articles available from online databases. Relevant articles published in other languages, in other databases and unpublished studies may have been missed, which might bias the results.

In conclusion, this meta-analysis suggested that PON1 polymorphisms were associated with PCOS risk.

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