

***XRCC1* gene rs25487, rs1799782 polymorphisms do not influence the susceptibility of CAD.**

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Abstract

Background: Two meta-analyses assessed the association between X-Ray Repair Cross Complementing 1 (*XRCC1*) gene polymorphisms and Coronary Artery Disease (CAD) risk. However, these two meta-analyses all included the studies without Hardy-Weinberg equilibrium (HWE). Therefore, their results were not reliable.

Methods: PubMed, EMBASE, MEDLINE, and the Cochrane Library were searched up to May 2017. Odds Ratios (OR) and 95% Confidence Interval (CI) were evaluated to determine the strength.

Results: Five case-control studies with 1715 cases and 1520 controls were included in this meta-analysis. A significant association was not found between *XRCC1* rs25487 polymorphism and CAD risk (OR=0.93; 95% CI, 0.72-1.21; P=0.61). No significant association was found between *XRCC1* rs25487 polymorphism and CAD risk in Caucasian (OR=0.93; 95% CI, 0.63-1.39; P=0.74) and Asian (OR=0.93; 95% CI, 0.50-1.75; P=0.83). A significant association was also not found between *XRCC1* rs1799782 polymorphism and CAD risk (OR=1.07; 95% CI, 0.92-1.25; P=0.39). In the Caucasian subgroup, no significant association was observed (OR=1.07; 95% CI, 0.92-1.25; P=0.39).

Conclusions: This meta-analysis suggested that *XRCC1* gene rs25487, rs1799782 polymorphisms were not associated with CAD risk.

Keywords: *XRCC1*, CAD, Polymorphism.

Accepted on August 21, 2017

Introduction

Coronary Artery Disease (CAD) is very common with a prevalence of 6.9% in males and 6% in females [1]. It is a multifactorial disease. Many reports suggested that this disease is resulting from interactions between environmental and genetic factors [2]. More recently, some studies indicated the role of genetic factor in CAD development [3].

The protein of X-ray Repair Cross Complementing 1 (*XRCC1*) play an important role in diseases development [4]. *XRCC1* gene polymorphisms were associated with disease susceptibility. Forat-Yazdi et al. found that Arg399Gln in *XRCC1* was associated with colorectal cancer risk [5]. Yan et al. suggested that this polymorphism was associated with the risk of prostate cancer [6]. Fan et al. suggested that the *XRCC1* Arg194Trp polymorphism was associated with the efficacy of platinum-based chemotherapy [7]. Sanjari et al. suggested that *XRCC1* gene polymorphisms were associated with breast cancer risk [8]. Previous studies have investigated the association between *XRCC1* gene polymorphisms and CAD risk [9-13]. Two meta-analyses also tried to determine the association between *XRCC1* gene polymorphisms and CAD risk [14,15]. Guo et al. suggested that the Arg194Trp polymorphism contributed to the CAD risk [14]. Ma et al. suggested that the *XRCC1* gene Arg194Trp and Arg399Gln

polymorphisms were associated with CAD susceptibility [15]. However, these two meta-analysis all included the studies without Hardy-Weinberg Equilibrium (HWE). Therefore, the results were not reliable.

Materials and Methods

Publications search

PubMed, EMBASE, MEDLINE, and the Cochrane Library were searched up to May 2017. The following terms were used: ("coronary artery disease" or "coronary heart disease") and ("X-ray repair cross complementing 1" or "*XRCC1*"). We also searched the references of the identified articles and relevant reviews.

Inclusion criteria

Case-control studies were considered to include in this meta-analysis. The case-control studies should have the genotype frequencies. Studies were excluded if they reported data overlapping with those of a larger study.

Extraction of data

Data were extracted as follow: first author, ethnicity, year, age, gender, the sample sizes, the polymorphisms.

Statistical analysis

Review Manager V.5.2 (The Cochrane Collaboration) was employed to analyse the pooled effects with Odds Ratio (OR) with 95% Confidence Interval (CI). The genotype distribution was assessed by Hardy-Weinberg Equilibrium (HWE). Heterogeneity was assessed using the χ^2 -base Q test the I^2 test. A P value less than 0.10 or an I^2 more than 50% suggests significant heterogeneity. We used the fixed effect model for pooled analysis preferentially; if high heterogeneity was

identified, we used the random effect model instead. We also did subgroup analyses according to race. Statistical significance was considered when a 2-tailed P value less than 0.05 was observed.

Results

Characteristics of the studies

Five studies (1715 cases and 1520 controls) were included in this study. Two case-control studies were done in Asians. Three case-control studies were done in Caucasians. All studies investigated rs25487 and two studies investigated rs1799782. Table 1 showed the main characteristics.

Table 1. Characteristics of the studies included in this meta-analysis.

Study	Year	Ethnicity	Age group	Gender	No. of case	No. of control	Polymorphisms
Bazo	2011	Caucasian	Adult	Mixed	117	52	rs25487, rs1799782
Gokkusu	2013	Caucasian	Adult	Mixed	197	135	rs25487
Narne	2013	Asian	Adult	Mixed	160	121	rs25487
Yu	2014	Asian	Adult	Mixed	1142	1106	rs25487
Hameed	2016	Caucasian	Adult	Mixed	99	106	rs25487, rs1799782

Table 2. Result of this meta-analysis.

Polymorphism	No. of studies	Test of association		Heterogeneity	
		OR (95% CI)	P value	I^2 (%)	P value
rs25487	5	0.93 (0.72-1.21)	0.61	76	0.002
Caucasian	3	0.93 (0.63-1.39)	0.74	74	0.02
Asian	2	0.93 (0.50-1.75)	0.83	88	0.004
rs1799782	2	1.07 (0.92-1.25)	0.39	53	0.15
Caucasian	2	1.07 (0.92-1.25)	0.39	53	0.15

Results of this study

The results are shown in Table 2. No significant association was found between *XRCC1* rs25487 polymorphism and CAD (OR=0.93; 95% CI, 0.72-1.21; P=0.61; Figure 1). When stratified by race, no significant association was found between *XRCC1* rs25487 polymorphism and CAD risk in Caucasian (OR=0.93; 95% CI, 0.63-1.39; P=0.74; Table 2) and Asian (OR=0.93; 95% CI, 0.50-1.75; P=0.83; Table 2). The shape of the funnel plot did not show obvious asymmetry (data not shown). A significant association was also not found between *XRCC1* rs1799782 polymorphism and CAD risk (OR=1.07; 95% CI, 0.92-1.25; P=0.39; Figure 2). In the Caucasian subgroup, no significant association was observed (OR=1.07; 95% CI, 0.92-1.25; P=0.39). Funnel plot also could not find obvious asymmetry.

Discussion

No significant association was found in this study. When stratified by race, *XRCC1* rs25487 polymorphism has not influence the CAD risk in Caucasian and Asian. Additionally, *XRCC1* rs1799782 polymorphism has not influence the CAD risk in Caucasian. Our results were different from the previous two meta-analyses [14,15]. Both of them found positive results. However, they included wrong studies. Thus, the results from their studies were not reliable.

XRCC1 Arg399Gln polymorphism was associated with hepatitis-related hepatocellular carcinoma [16]. Jiang et al. suggested that pancreatic cancer risk was associated with *XRCC1* rs25487 polymorphism in Asians [17]. Wang et al.

Figure 1. The association between *XRCC1* rs25487 polymorphism and CAD risk.

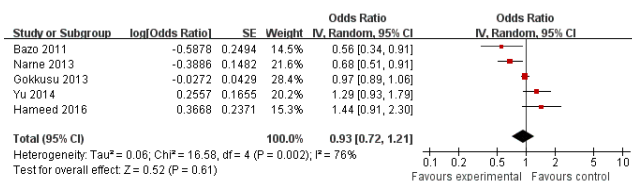
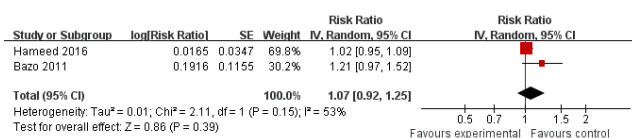


Figure 2. The association between *XRCC1* rs1799782 polymorphism and CAD risk.



suggested that lung cancer risk in Asian population was associated with *XRCC1* 399 polymorphism [18]. Yang et al. indicated that bladder cancer might be associated with *XRCC1* rs25487 polymorphism [19]. Chen et al. concluded that laryngeal cancer was not associated with *XRCC1* Arg399Gln polymorphism [20].

Some limitations should be addressed. First, more case-control studies are needed to assess the results in different races. Second, publication bias cannot be ruled out. Third, we did not perform other subgroup analyses due to limited data.

In conclusion, this meta-analysis suggested that *XRCC1* gene rs25487, rs1799782 polymorphisms were not associated with CAD risk.

Disclosure of Conflict of Interest

The authors have declared that no competing interests exist.

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