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X-ray repair cross-complementing group 3 common polymorphism is not associated with cervical cancer risk.

Yi Cao[1*#], Wei Chen[1#], Yi Xia[2], Ge Zhao[3], Zheng Hu[1], Xin-Hua Xie[1]

[1]Department of Obstetrics and Gynecology, the Minhang Hospital of Fudan University, the Central Hospital of Minhang District, 170 Xin Song Road, Shanghai, PR China

[2]Department of Radiation Oncology, Fudan University, Shanghai Cancer Center, Minhang Branch, Shanghai, PR China

[3]Department of Anesthesia, the First Hospital of Xi'an Jiao Tong University, Shanxi, PR China

[#]These authors contributed equally to this study

Abstract

Recently, some reports investigated the association between X-ray Repair Cross-Complementing group 3 (XRCC3) and cervical cancer risk. However, the results were inconclusive. The meta-analysis, thus, assessed whether XRCC3 T241M polymorphism was associated with cervical cancer risk. Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were calculated. Five case-control studies with a total of 806 cervical cancer cases and 850 controls were included. No association between XRCC3 T241M polymorphism and cervical cancer risk was found. In subgroup analysis, Asians with this polymorphism seemed to be associated with cervical cancer risk. Publication bias was not performed. In conclusion, this meta-analysis suggested that XRCC3 T241M polymorphism was not associated with cervical cancer risk.

Keywords: Cervical cancer, X-ray repair cross-complementing group 3, Meta-analysis, Polymorphism.

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Introduction

Cervical cancer ranks as the third most common female cancer worldwide, and is the leading cause of death from cancer among women in developing countries [1]. Although the medical situation has improved, the incidence and mortality rate of cervical cancer are still increasing in parts of developing countries. Despite the improvement in diagnostic and therapeutic strategies, the 5 y survival rate for patients with advanced stage cervical cancer remains poor [2].

X-ray Repair Cross-Complementing group 3 (XRCC3) is involved in maintaining the stability of genome by homologous recombination repair for DNA double-strand breaks [3]. XRCC3 T241M polymorphism has a critical role in the development of cancers and many diseases. Sobhan et al. revealed a significant association between the XRCC3 rs861539 polymorphism and risk of osteosarcoma, especially in Asian populations [4]. Ji et al. suggested that XRCC3 T241M polymorphism may constitute a risk factor for hepatocellular carcinoma in the Chinese population [5]. Lu et al. concluded that the XRCC3 Thr241Met polymorphism is associated with an increased risk of thyroid cancer [6]. Ali et al. suggested that rs1799794 in XRCC3 shows strong association with breast cancer development in Saudi females [7]. Recently, some reports investigated the association between X-ray repair cross-complementing group 3 (XRCC3) and cervical cancer risk [8-12]. However, the results were inconclusive. The meta-analysis, thus, assessed whether XRCC3 T241M polymorphism was associated with cervical cancer risk.

Materials and Methods

Search relevant studies

We searched PubMed, EMBASE, and Wangfang databases. The key terms were used as: (XRCC3 or 'X-ray repair cross-complementation group 3') and (cervical cancer). No language restrictions were applied.

Inclusion and exclusion criteria

A study was included in the current meta-analysis if: (1) it was a case-control study, (2) genotype distributions in both cases and controls should be available for estimating an Odds Ratio (OR) with 95% Confidence Interval (CI). Studies were excluded if any of the following conditions applied: (1) only abstracts or reviews were available, without sufficient data; (2) genotype frequencies were not reported; (3) studies were repeated or publications overlapped.

Data extraction

Two investigators independently extracted data: the first author's name, year of publication, ethnicity of the study population, numbers of cases and controls.

Statistical analysis

The strength of association was assessed by calculating OR with 95% CI. The pooled ORs were performed for dominant model. Stratified analysis was performed by ethnicity. Departure from Hardy-Weinberg Equilibrium (HWE) in controls was tested by the chi-square test. The Q statistic and the I^2 statistic were used to assess the degree of heterogeneity among the studies included in the meta-analysis. If heterogeneity was observed among the studies, the random-effects model was used to estimate the pooled OR (the Dersimonian and Laird method). All statistical tests were performed with the software Revman 5.1 software (Nordic Cochrane Center, Copenhagen, Denmark). A P value<0.05 was considered statistically significant.

Results

Characteristics of studies

A total of 5 case-control studies with 806 cervical cancer cases and 850 controls were included for this meta-analysis. There were 3 studies of Asian population and 2 studies of Caucasian population. All studies suggested that the distribution of genotypes in the controls was consistent with HWE. The characteristics of each case-control study are presented in Table 1.

Table 1. *Characteristics of the included studies.*

First author	Country	Ethnicity	Age	HPV	Case number (n)	Control number (n)	Hardy-Weinberg equilibrium
He	China	Asian	Adult	Mixed	200	200	Yes
Xiao	China	Asian	Adult	Mixed	158	164	Yes
Settheetham-Ishida	USA	Asian	Adult	Mixed	111	118	Yes
Pérez	China	Caucasian	Adult	Mixed	117	205	Yes
Djansugurova	China	Caucasian	Adult	Mixed	217	160	Yes

Results of meta-analyses

A random-effect model was used for synthesis of the data. The overall OR was 1.34 (95% CI, 0.89-2.01). Subgroup analysis by ethnicity was performed. There was no significant association with cervical cancer risk in Caucasian. However, Asians with this polymorphism seemed to be associated with cervical cancer risk.

Publication bias

Only 5 case-control studies were included in this meta-analysis. Thus, we did not perform to access the publication bias.

Discussion

This meta-analysis included 5 case-control studies with 806 cervical cancer cases and 850 controls. We did not find a significant association between XRCC3 T241M polymorphism and cervical cancer risk. There was also no significant association with cervical cancer risk in Caucasian. However, Asians with this polymorphism seemed to be associated with cervical cancer risk.

Zeng et al. indicated that the XRCC1 Arg399Gln polymorphism decreased the risk of cervical cancer [13]. Yang et al. suggested that AT haplotype in the *ITPR3* gene may serve as a potential marker for genetic susceptibility to cervical squamous cell carcinoma [14]. Zhao et al. suggested that the GSTP1 Ile105Val polymorphism is not associated with the development of gynecological cancer [15]. Rotar et al. suggested that no link has been found between VEGF+936 C/T and cervical intraepithelial neoplasia [16].

Some limitations should be acknowledged. First, lacking of the original data of the eligible studies limited the evaluation of the effects of the gene-gene and gene-environment interactions in the development of cervical cancer. Second, potential publication bias might exist. Third, the included studies did not control all covariates.

In conclusion, no association between the XRCC3 T241M polymorphism and cervical cancer risk was found in this study.

Conflicts of Interest

None

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*Correspondence to

Yi Cao

Department of Obstetrics and Gynecology

The Minhang Hospital of Fudan University

The Central Hospital of Minhang District

PR China