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XRCC1 rs1799782 polymorphism and objective response rate in NSCLC patients treated with platinum-based chemotherapy.

Peng-Cheng Wang[#], Xing Du[#], Yi Wang, Xiao-Li Zheng[*]

Department of Pharmacy, the Affiliated Yantai Yuhuangding Hospital of Qingdao University, Yantai 264000, PR China

[#]These authors contributed equally to this work.

Abstract

Background: Some previous studies suggested that *XRCC1* rs1799782 polymorphism was associated with the objective response rate (ORR) of platinum-based chemotherapy. However, the results were not coincident. Thus, we conducted this meta-analysis.
Methods: The databases of PubMed, Embase, Cochrane Library, and Web of Science were searched. This meta-analysis was performed using Stata version 12.0 (StataCorp LP, TX, USA).
Results: In this meta-analysis study, a total of 13 relevant articles with 2540 NSCLC patients were enrolled. Results of this meta-analysis study showed that the NSCLC patients with *XRCC1* rs1799782 Trp/Trp genotype were associated with worse ORR (OR=1.37; 95%CI, 1.01-1.79). In addition, *XRCC1* rs1799782 Arg/Trp genotype was associated with worse ORR (OR=1.41; 95%CI, 1.14-1.75). Furthermore, NSCLC patients with *XRCC1* rs1799782 Trp/Trp or Arg/Trp genotype also showed worse ORR (OR=1.39; 95%CI, 1.02-1.76).
Conclusions: In conclusion, this meta-analysis suggested that *XRCC1* rs1799782 polymorphism was significantly associated with ORR in NSCLC patients treated with platinum-based chemotherapy.

Keywords: *XRCC1*, NSCLC, Objective response rate, Chemotherapy.

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Introduction

Lung cancer is one of the leading causes of cancer-associated mortality. Non-small cell lung cancer (NSCLC) accounts for 80–85% of all lung cancer-associated mortalities [1]. Although a great number of therapeutic methods were extensively explored in clinical application, it has been verified that systemic chemotherapy can provide promising improvement in both survival rate and life quality for NSCLC patients [2]. X-ray repair cross complementing 1 (*XRCC1*) located at chromosome 19q13.2, is a key component of base excision repair (BER) and is required for genetic stability [3]. The *XRCC1* gene codes for a DNA-repair enzyme that is involved in base excision repair of oxidative DNA damage as well as single-strand break repair. Evidence has shown that polymorphisms in DNA repair genes could influence individual DNA repair capacity [4]. Lu et al. suggested that *XRCC1* Arg194Trp polymorphism was associated with increased risk for glioma, especially in Asians [5]. Yang et al. indicated that no association between *rs25487* or *rs1799782* gene polymorphism and risk of female reproductive cancer risk was found [6]. Jafari Nedooshan et al. found an increased risk of thyroid cancer with the *XRCC1* rs1799782 and rs25487 polymorphisms [7]. Wang et al. suggested that Chinese Han people with rs1799782 TT/CT genotype of *XRCC1* gene may have increased risk of developing colorectal cancer [8]. Some previous studies suggested that *XRCC1* rs1799782 polymorphism was associated with the objective response rate (ORR) of platinum-based chemotherapy [9-21]. However, the results were not coincident. Thus, we conducted this meta-analysis.

Materials and Methods

Publications Search

The databases of PubMed, Embase, Cochrane Library, and Web of Science were searched. Search terms included "X-ray repair cross complementing 1," "*XRCC1*," " non-small cell lung cancer," "chemotherapy," and "NSCLC." Duplicated studies were excluded. Titles and abstracts were scanned thoroughly to exclude irrelevant articles. Finally, all of the full texts of the remaining articles were assessed comprehensively to identify the studies that contained the topic of interest.

Inclusion criteria and Data extraction

Inclusion criteria were as follows: (1) case-control or cohort studies; (2) NSCLC based on histopathological confirmation; (3) focused on the ORR of chemotherapy. The exclusion criteria were (1) non-English papers; (2) review articles, editorial comments, letters, expert opinion, conference

abstracts, or case reports. Data were extracted as follow: first author, year, country, ethnicity, and the sample sizes.

Statistical analysis

This meta-analysis was performed using Stata version 12.0 (StataCorp LP, TX, USA). For the analysis of the relationship between ORR and *XRCC1* rs1799782 polymorphism, ORs and 95% CIs were considered effective values. Heterogeneity among the studies was determined through Q and I2 tests. All p-values were two sided, and statistical significance was set at $p<0.05$.

Results

Characteristics of the studies

As shown in Table 1, we identified 13 relevant articles through combined manual and computerized retrieval. Five studies were conducted in Caucasians and 8 studies were conducted in Asians. The sample sizes in each study ranged 82 to 378. Finally, a total of 2540 NSCLC patients were enrolled.

Table 1. *The characteristics of the included cohort studies.*

Author/ Year	Country	Ethnicity of subjects	Number of subjects
Gurubhagavatula/2004	USA	Caucasian	103
de las Penas/2006	Spain	Caucasian	135
Giachino/2007	Italy	Caucasian	249
Sun/2009	China	Asian	82
Hong/2009	China	Asian	164
Qiu/2009	China	Asian	107
Xu/2011	China	Asian	130
Joerger/2012	Netherlands	Caucasian	131
Zhao/2013	China	Asian	147
Sullivan/2014	Spain	Caucasian	161
Jin/2014	China	Asian	378
Liu/2014	China	Asian	378
Zhang/2014	China	Asian	375

Results of meta-analysis

Results of this meta-analysis study showed that the NSCLC patients with *XRCC1* rs1799782 Trp/Trp genotype were associated with worse ORR (OR=1.37; 95%CI, 1.01-1.79). In addition, *XRCC1* rs1799782 Arg/Trp genotype was associated with worse ORR (OR=1.41; 95%CI, 1.14-1.75). Furthermore, NSCLC patients with *XRCC1* rs1799782 Trp/Trp or Arg/Trp genotype also showed worse ORR (OR=1.39; 95%CI, 1.02-1.76).

Discussion

In this meta-analysis study, a total of 13 relevant articles with 2540 NSCLC patients were enrolled. Results of this meta-analysis study showed that the NSCLC patients with *XRCC1* rs1799782 Trp/Trp genotype were associated with worse ORR. In addition, *XRCC1* rs1799782 Arg/Trp genotype was associated with worse ORR. Furthermore, NSCLC patients with *XRCC1* rs1799782 Trp/Trp or Arg/Trp genotype also showed worse ORR. Putthanachote et al. suggested that *XRCC1* gene homozygosity, particularly Arg/Arg, on the risk for stomach cancer was elevated by a high intake of vegetable oils and salt [22]. Zhai et al. found that there are no correlations between *XRCC1* genotypes and ovarian carcinoma survival [23]. Zhang et al. indicated that *XRCC1* Arg399Gln GA variant might be risk alleles for cervical cancer susceptibility in the Chinese population [24]. Wang et al. suggested that *XRCC1* rs25487 A allele with bad survival for advanced NSCLC in Chinese population [25]. Sanjari Moghaddam et al. suggest that *XRCC1* gene polymorphisms modify breast cancer risk in different populations and different categories of menopausal status [26].

This meta-analysis has several limitations. First, the quality of all the included trials in this meta-analysis was low. Second, we did not perform subgroup analyses by ethnicity and gender. Third, the sample size was also relatively small in the included studies. In conclusion, this meta-analysis suggested that *XRCC1* rs1799782 polymorphism was significantly associated with ORR in NSCLC patients treated with platinum-based chemotherapy.

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***Correspondence to**

Xiao-Li Zheng

Department of Pharmacy

The Affiliated Yantai Yuhuangding Hospital of Qingdao University

PR China