Research Article

Association between ERCC1 Gene Polymorphism (rs11615) and Colorectal Cancer Susceptibility: A Meta-Analysis of Medical Image Fusion and Safety Applications

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Abstract

Colorectal cancer (CRC) is a malignant tumor of the colorectal mucosa epithelial tissue transformed. The fusion of data for medical imaging has become a central issue in such biomedical applications as image-guided surgery and radiotherapy. Currently, CRC has been one of the most threatening tumors affecting people’s health worldwide. The excision repair cross-complementation group 1 (ERCC1) is a key enzyme for nucleotide excision repair (NER). Emerging epidemiological studies have indicated that the presence of colorectal cancer (CRC) may be relevant to the ERCC1 rs11615 genetic polymorphism. However, the results of ERCC1 rs11615 on CRC in these studies are controversial. We searched PubMed, Web of Science, Embase, CNKI, and CBM databases for the effects of ERCC1 rs11615 variant on CRC development. There was no meta-analysis focused on the diagnosis of colorectal cancer with ERCC1 rs11615 variant. We creatively carried out a meta-analysis of nine case-control studies and used Stata (version 12.0) software to integrate the pooled odds ratios (ORs) corresponding to a 95% confidence interval (CI) of overall and subgroup analysis. Our results suggest that a significant correlation was observed between rs11615 and the susceptibility of CRC OR 95% CI = 1.13 (1.04-1.23) under an allele genetic model and OR 95% CI = 1.14 (1.01-1.30) under a dominant genetic model for overall CRC. Significant statistical difference was also noted in Asians rather than Caucasians based on the ethnicity subgroups. These results suggested that there is a certain association between rs11615 and the susceptibility of colorectal cancer in the Asian populations.

1. Introduction

Colorectal cancer (CRC) is a malignant tumor of the colorectal mucosa epithelial tissue transformed. It is transformed under the factors of genes, diets, environment, and other pathogenic reasons [1]. According to the GLOBOCAN 2016 database, colorectal cancer (CRC) was the third most common cancer accounting for 8% of death among all sites of cancers in the United States [2]. Recurrence and metastasis are the most important causes of death. In the past 20 years, the death rate of CRC decreased continuously in America. However, we cannot ignore a large number of deaths [2]. What is more, CRC morbidity and mortality in China is on the rise in recent years [3]. Currently, CRC has been one of the most threatening tumors affecting people’s health worldwide. Many studies have confirmed that not only are dietary habits, environmental factors, and chronic inflammation of the intestinal tract primary elements of colorectal cancer, but the pathogenesis is also influenced by genetic control. Accumulation of DNA damages can cause genomic instability and mutations. Fortunately, 4 major pathways can remove or repair DNA damage, including nucleotide excision repair (NER), mismatch repair (MMR), base excision repair (BER), and double-strand break repair [4]. Repair of DNA was verified to be critical in protecting from cancer-causing agents initially in xeroderma pigmentosum (XP), and subsequently in colon cancer [5]. Mutations of NER-related genes have caused a wide
range of attention [6]. ERCC1, as one of the most important rate-limiting enzymes in NER, maps to chromosome 19q13.2~13.3, length 15 kb, composed of 10 exons, encoding a containing 297 ammonia [7]. So far, many studies have shown that mutations of single nucleotide polymorphisms (SNP) of ERCC1 are associated with multiple types of tumors susceptibility and prognosis [8–12]. A common SNP of ERCC1 gene is located at 118 codon of T > C (rs11615, Asn118Asn). As one of the most common SNP of ERCC1, rs11615 polymorphism, a base substitution of ancestral allele C to mutation allele T, has been demonstrated that modify the risk for various cancers, for example, non-small-cell lung cancer, glioma and meningioma, esophageal adenocarcinoma, and gynecology tumors like ovarian and cervical cancer [12–17].

In the past decade, extensive researches were done to find the biomarker for screening for colorectal cancer [18]. However, it needs further exploration. What is more, due to the rapid diagnosis of prostate cancer, the overall cancer incidence declined from 2009 to 2012 [2]. Early screening can decrease the mortality and incidence of colorectal cancer. It can also remove precancerous lesions [19]. Early diagnoses of cancer and precancerous prevention are necessary. Some epidemiological studies have explored the relationship between the susceptibility of CRC and ERCC1 rs11615 variant. Nevertheless, evidence was limited, and the result was

**Table 1**: Characteristics of nine eligible studies.

| First author | Year | Ethnicity | Country | Case CC1 | Case CT1 | Case TT1 | Total Case | Control CC0 | Control CT0 | Control TT0 | Total Control | Genotyping | HWE | Source of control |
|--------------|------|-----------|---------|----------|----------|----------|------------|-------------|-------------|-------------|---------------|------------|-----|------------------|
| Hansen       | 2008 | Caucasians | DANISH  | 61       | 166      | 168      | 395        | 113         | 349         | 333         | 795          | PRC-RFLP   | 0.165 | PB               |
| Hou          | 2014 | Asians     | CHINA   | 73       | 94       | 37       | 204        | 85          | 90          | 29          | 204          | PRC-RFLP and MALDI-TOF MS | 0.514 | HB |
| Ni           | 2014 | Asians     | CHINA   | 117      | 82       | 14       | 213        | 135         | 86          | 19          | 240          | TaqMan     | 0.315 | HB               |
| Skjeldred    | 2006 | Caucasians | NORWAY  | 21       | 64       | 68       | 153        | 66          | 185         | 140         | 391          | PRC-RFLP   | 0.714 | PB               |
| Yang         | 2015 | Asians     | CHINA   | 108      | 121      | 50       | 279        | 134         | 133         | 49          | 316          | PRC-RFLP   | 0.100 | HB               |
| Yueh         | 2017 | Asians     | CHINA   | 160      | 131      | 71       | 362        | 180         | 139         | 43          | 362          | TaqMan     | 0.049 | HB               |
| Gomez        | 2015 | Caucasians | MEXICO  | 46       | 47       | 15       | 108        | 58          | 50          | 11          | 119          | TaqMan     | 0.962 | HB               |
| Moreno       | 2006 | Caucasians | SPAIN   | 132      | 138      | 64       | 334        | 123         | 126         | 52          | 301          | PRC-RFLP   | 0.049 | HB               |
| Gil          | 2012 | Caucasians | POLISH  | 13       | 78       | 42       | 133        | 16          | 48          | 36          | 100          | PRC-RFLP   | 1.000 | HB               |

PB: Population-based. HB: Hospital-based.
inconclusive. The study of Yueh et al. told us the risk of colorectal cancer increased 1.86-fold in people carrying TT genotype on the rs11615 site. They consider the genome becomes unstable if the ERCC1 gene is mutated [20]. The level of mRNA and protein reduced subsequently before cancer happened. But Yang et al. discredited these conclusions [21]. In his study, ERCC1 rs2298881 polymorphism rather than rs11615 is associated with an increased risk of colorectal cancer; (2) using a meta-analysis or system review; (3) diagnosis of patients is not clear; (4) frequency in each genotype or some important data are not extractable.

Two researchers (Zhifeng Qiu and Min Liu) screened all records independently on the basis of inclusions and exclusions and conducted independent data extraction. They asked help from the third person (Wen Liu) if there is a dispute. We discussed to reach a consensus. If reports are from the same center or cohort study, we will adopt the one which was the most recent one or most participants.

### 2. Materials and Methods

#### 2.1. Search Strategy

A search strategy of literature with the following keywords: (“colorectal neoplasms” or “colorectal cancer” or “colon-rectal cancer”), (“Excision repair cross-complementation group 1” or “ERCC1”), and (“polymorphism” or “genotype” or “variant” or “SNP”) were utilized to search in various databases. We searched keywords in PubMed, Embase, Web of Science, and CNKI, CBM in English or Chinese, respectively. Two authors finished the search independently, and the final search was until the date of July 2017. Publications in English or Chinese were checked. We also checked related references to included studies to find out if there are any other potentially eligible essays.

#### 2.2. Selection Criteria

We will intake the publication if it satisfied with following conditions: (1) studies that assessed the polymorphism of ERCC1 rs11615 in CRC patients; (2) using a case-control study or cohort study design; (3) patients in case group are diagnosed with cancer, and populations in control group or based populations are unrelated with CRC clearly, without limit of age, gender, and nationality; (4) each group has described the frequency of genotype in detail; (5) showed data of an odd ratio (OR) with corresponding 95% confidence interval (CI); (6) provided details of detection technology of genotype.

Exclusion criteria: (1) the claim of the study did not mention the relationship of ERCC1 rs11615 polymorphism with colorectal cancer; (2) a meta-analysis or system review; (3) diagnosis of patients is not clear; (4) frequency in each genotype or some important data are not extractable.

#### 2.3. Data Extraction

We extracted the frequency in each genotype from eligible studies. The first author’s name, the year of publication, the object of study in different races, the study design, sample quantity of case and control, based populations, the method of genotyping, and sample source are also extracted by the two authors independently.

#### 2.4. Statistical Analysis

We made use of odds ratios (ORs) corresponding to a 95% confidence interval (CI) to assess the strength of the link between ERCC1 rs11615 genotype allele T mutation and CRC compared to allele C. Homozygote model (TT vs. CC), dominant model (TT + TC vs. CC), recessive model (TT vs. TC + CC), and allele model (T vs. C) were applied. We recalculated the ORs after stratification of the ethnicity or other factors that may impact the result. The pool ORs was calculated by the random-effect model. Otherwise, we chose a fixed model [22]. Egger’s test and funnel plot were applied to evaluate publication bias. We did the sensitivity analysis to evaluate the stability of results.

### Table 2: Summary of ORs (95% CI) with heterogeneity test for ERCC1 rs11615 polymorphism and CRC cancer risk under several genetic models.

| Subgroup                  | No. of studies | T vs. C OR (95% CI) | $I^2$ | TT + TC vs. CC OR (95% CI) | $I^2$ | TT vs. TC + CC OR (95% CI) | $I^2$ | TT vs. CC OR (95% CI) | $I^2$ |
|---------------------------|----------------|---------------------|------|---------------------------|------|---------------------------|------|---------------------|------|
| Racial descent            |                |                     |      |                           |      |                           |      |                     |      |
| Asian                     | 4              | 1.19 (1.05-1.35)$^b$| 0    | 1.19 (1.00-1.41)$^b$      | 0    | 1.36 (1.06-1.73)$^b$      | 28   | 1.43 (1.10-1.85)$^b$   | 16.7 |
| Caucasian                 | 5              | 1.08 (0.97-1.21)    | 0    | 1.09 (0.90-1.32)         | 0    | 1.11 (0.94-1.32)         | 0.7  | 1.16 (0.92-1.46)      | 0    |
| Source of control         |                |                     |      |                           |      |                           |      |                     |      |
| Population-based          | 2              | 1.10 (0.85-1.42)    | 60$^a$| 1.01 (0.76-1.34)         | 11.6 | 1.17 (0.85-1.62)         | 52.4 | 1.14 (0.71-1.82)      | 50.7$^a$|
| Hospital-based            | 7              | 1.16 (1.05-1.29)$^b$| 0    | 1.18 (1.03-1.36)$^b$     | 0    | 1.24 (1.03-1.50)$^b$     | 18.5 | 1.37 (1.12-1.70)$^b$  | 0    |
| HWE                       |                |                     |      |                           |      |                           |      |                     |      |
| <0.05                     | 2              | 1.20 (0.96-1.50)    | 50.1$^a$| 1.16 (0.93-1.44)         | 0    | 1.43 (0.91-2.26)         | 60.3$^a$| 1.46 (0.91-2.35)    | 57.1$^a$|
| ≥7.1                      | 7              | 1.10 (1.00-1.22)    | 0    | 1.14 (0.97-1.33)         | 0    | 1.12 (0.96-1.32)         | 0    | 1.19 (0.97-1.47)      | 0    |
| Overall                   | 9              | 1.13 (1.04-1.23)$^b$| 0    | 1.14 (1.01-1.30)$^b$     | 0    | 1.19 (1.03-1.37)$^b$     | 18.8 | 1.27 (1.07-1.51)$^b$  | 3.3  |

$^a$: Random effect estimate. $^b$: Significant results, $P < 0.05$. 

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**Table 2: Summary of ORs (95% CI) with heterogeneity test for ERCC1 rs11615 polymorphism and CRC cancer risk under several genetic models.**
2.5. Medical Image Security Applications. Medical image security is an important issue when digital images and their pertinent patient information are transmitted across public networks. There are ethical and legal obligations for health care providers to preserve the privacy and confidentiality of patient information, which can contain some of the most intimate information conceivable about an individual. Despite the advantages of electronic medical records (EMR), there is a higher chance of disclosure of information to the public compared to other formats such as paper-based records. Three aspects of security arise in relation to dealing with medical images: confidentiality, reliability, and availability.

3. Results

3.1. Characteristics of Eligible Studies. Six hundred and eighty-nine articles were found after entering key terms. But only 33 articles were chosen to enter the full-text view phase. Finally, 9 case-control studies, including 2,181 clear-diagnosed cases and 2,828 controls, were analyzed after discarding reviews, duplicates, or those fail to meet the inclusion standards. Details for the literature search and screen were presented in Figure 1. Characteristics of eligible studies have summarized in Table 1. Five studies were conducted in Caucasian populations and four in Asian populations [16–19]. Studies have mentioned that the gender and sex were matched between the case and control group [20, 21, 23–26]. Among these studies, sources of controls were healthy people or hospital-based shown in Table 1. In addition, blood samples for genotyping were used in all studies. The genotype of ERCC1 rs11615 polymorphism was determined using three methods. The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) and TaqMan assay were conducted in nearly all the publications. Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) was also used in the study of Hou et al. [24]. The genotype distributions were in agreement with HWE (P > 0.05) among seven studies, but not in the study of Yueh et al. and Moreno et al. (P = 0.049 < 0.05) [20, 25].

3.2. Meta-Analysis Results. In this merge meta-analysis, all results of the test for association and heterogeneity were displayed in Table 2. It was detected that significant link occurred between T allele variant in ERCC1 rs11615 site and colorectal carcinoma when every study was pooled into the meta-analysis, containing four genetic models (Table 2, Figure 2), an allele model (OR = 1.13, 95% CI = 1.04 – 1.23, P = 0.004, Heterogeneity = 0.51, and I² = 0%), a dominant model (OR = 1.14, 95% CI = 1.01 – 1.30, P = 0.037, Heterogeneity = 0.82, and I² = 0%), a recessive model (OR = 1.19, 95% CI = 1.03 – 1.37, P = 0.015, Heterogeneity = 0.28, and I² = 18.8%), and a homozygote model (OR = 1.27, 95% CI = 1.07 – 1.51, P = 0.006, Heterogeneity = 0.41, and I² = 3.3%). Stratification by ethnicity confirmed that subjects carrying T genotype increase significantly associated with CRC in Asians. This significance was also found in other genetic models (dominant model: OR = 1.19, 95% CI = 1.00 – 1.41, P = 0.046, Heterogeneity = 0.88, and I² = 0.00%; recessive model: OR = 1.36, 95% CI = 1.06 – 1.73, P = 0.014, Heterogeneity = 0.24, and I² = 28.00%; homozygote model: OR = 1.43, 95% CI = 1.10 – 1.85, P = 0.007, Heterogeneity = 0.31, and I² = 16.7%). However, these associations cannot be found in Caucasians, under any contract model. OR = 1.08, 95% CI = 0.97 – 1.21, Heterogeneity = 0.51, and I² = 0% under the allele model; OR = 1.09, 95% CI = 0.90 – 1.32, Heterogeneity = 0.51, and I² = 0% under the dominant model; OR = 1.11, 95% CI = 0.94 – 1.32, Heterogeneity = 0.4, and I² = 0.7% under the recessive model; OR = 1.16, 95% CI = 0.92 – 1.46, Heterogeneity = 0.51, and I² = 0% under the homozygote model. We reanalyzed based on in accordance with HWE. It came out that no significant association between rs11615 polymorphism and colorectal cancer susceptibility.

3.3. Publication Bias and Sensitivity Analysis. With the OR-value as the abscissa, the standard deviation of the log (OR) as the ordinate to draw funnel plots. As displayed in Figure 3, roughly symmetrical was found among studies. And then, proceed to Egger’s test. The results are t = 1.77 and P = 0.12 under a dominant model and t = 0.76 and P = 0.473 under an allele model (data not shown). In the Begg’s test, Pr > |z| = 0.348 (continuity corrected) under a dominant model, Pr > |z| = 0.754 (continuity corrected) under an allele model. Begg’s funnel plots of other genetic models were shown in Figure 3. In summary, publication bias in this meta-analysis is low. Sensitivity analyses told us that there is no single study that obviously influenced the main result of the summary OR (shown in Figure 4).

4. Discussion

The incidence of colorectal cancer between the ages of 30-50 was 50/105 yearly. And the number was double in the age of 50-70. Gradually it rose four times at ages > 70 years [27]. Currently, CRC has been one of the most threatening tumors affecting people’s health worldwide. Depending on statistics in America, the mortality of colorectal cancer has markedly dropped owing to carrying out asymptomatic census vigorously. Indeed, it is a matter of utmost urgency to improve the early diagnosis level of colorectal carcinoma in young people to improve the prognosis of patients.

Nucleotide excision repair is a momentous pathway to repair damages in no matter brought about by endogenic or exogenous reasons. ERCC1-XPF is not similar to other proteins. As a specific endonuclease, it cuts 5’ of the damaged segment in NER. It is also to the recombination and repair of DNA interstrand cross-links [28]. The results of phenotype lead to more serious mutations of ERCC1 or
Overall ($I^2 = 0.0\%, \ p = 0.508$)

| Study ID          | OR (95% CI) | Weight |
|-------------------|-------------|--------|
| Asians            |             |        |
| Hou (2014)        | 1.23 (0.93, 1.63) | 8.50   |
| Ni (2014)         | 1.00 (0.74, 1.35) | 8.45   |
| Yang (2015)       | 1.14 (0.90, 1.44) | 12.78  |
| Yueh (2017)       | 1.34 (1.08, 1.67) | 13.69  |
| Overall ($I^2 = 0.0\%, \ p = 0.513$) | 1.13 (1.04, 1.23) | 100.00 |

| Study ID          | OR (95% CI) | Weight |
|-------------------|-------------|--------|
| Caucasians        |             |        |
| Hansen (2008)     | 0.99 (0.83, 1.18) | 23.99  |
| Skjelbred (2006)  | 1.29 (0.98, 1.69) | 8.85   |
| Gomez (2015)      | 1.28 (0.86, 1.89) | 4.31   |
| Moreno (2006)     | 1.07 (0.85, 1.34) | 14.22  |
| Gil (2012)        | 1.04 (0.71, 1.51) | 5.23   |
| Subtotal ($I^2 = 0.0\%, \ p = 0.443$) | 1.19 (1.05, 1.35) | 43.41  |

Allele model

| Study ID          | OR (95% CI) | Weight |
|-------------------|-------------|--------|
| Caucasians        |             |        |
| Hansen (2008)     | 0.91 (0.65, 1.27) | 15.66  |
| Skjelbred (2006)  | 1.28 (0.75, 2.17) | 5.62   |
| Gomez (2015)      | 1.28 (0.76, 2.16) | 5.54   |
| Moreno (2006)     | 1.06 (0.77, 1.45) | 16.58  |
| Gil (2012)        | 1.76 (0.80, 3.85) | 2.10   |
| Subtotal ($I^2 = 0.0\%, \ p = 0.508$) | 1.09 (0.90, 1.32) | 45.50  |

| Study ID          | OR (95% CI) | Weight |
|-------------------|-------------|--------|
| Asians            |             |        |
| Hou (2014)        | 1.28 (0.86, 1.91) | 9.54   |
| Ni (2014)         | 1.05 (0.73, 1.53) | 12.15  |
| Yang (2015)       | 1.17 (0.84, 1.62) | 14.80  |
| Yueh (2017)       | 1.25 (0.93, 1.67) | 18.02  |
| Overall ($I^2 = 0.0\%, \ p = 0.883$) | 1.19 (1.00, 1.41) | 54.50  |

Dominant model

| Study ID          | OR (95% CI) | Weight |
|-------------------|-------------|--------|
| Caucasians        |             |        |
| Hansen (2008)     | 1.00 (0.77, 1.28) | 16.58  |
| Skjelbred (2006)  | 1.28 (0.98, 1.65) | 8.85   |
| Gomez (2015)      | 1.28 (0.86, 1.89) | 4.31   |
| Moreno (2006)     | 1.07 (0.85, 1.34) | 14.22  |
| Gil (2012)        | 1.04 (0.71, 1.51) | 5.23   |
| Subtotal ($I^2 = 0.0\%, \ p = 0.443$) | 1.19 (1.05, 1.35) | 43.41  |

| Study ID          | OR (95% CI) | Weight |
|-------------------|-------------|--------|
| Asians            |             |        |
| Hou (2014)        | 1.28 (0.86, 1.91) | 9.54   |
| Ni (2014)         | 1.05 (0.73, 1.53) | 12.15  |
| Yang (2015)       | 1.17 (0.84, 1.62) | 14.80  |
| Yueh (2017)       | 1.25 (0.93, 1.67) | 18.02  |
| Overall ($I^2 = 0.0\%, \ p = 0.820$) | 1.14 (1.01, 1.30) | 100.00 |

Figure 2: Continued.
XPF than the absence of NER [29]. When the ERCC-XPF is mutated, the capacity of DNA repair decreases and leads to a susceptibility to various decreases such as diverse cancers, genetic disorders Xeroderma pigmentosum (XP), Fanconi anemia (FA), and so on [30–33]. In 2011, Borgesius et al. have used a mouse model mutated with ERCC1 gene to approve that defects of ERCC1 impel acceleration of cognitive decline too [34].
Figure 3: Continued.
This meta-analysis is an attempt to analyze the potential correlation between the genetic variant of ERCC1 rs11615 and colorectal cancer as well. In this merged analysis, we demonstrated that the susceptible risk of colorectal cancer was associated with the TT variant of ERCC1 Asn118Asn (rs11615) and TC heterozygote compared to wild-type CC homozygote in the overall population. It is the same as Gil et al.’s observation that interaction existed between genotypes of T allele mutant site and morbidity of CRC [35]. However, Skjelbred et al. found that there was no association between the rs11615 polymorphism and the risk of CRC [36]. Gil et al. demonstrated that no evidence for a relationship between ERCC1 rs11615 variant and susceptibility of CRC as well. We have identified that studies of eastern countries contributed to the heterogeneity. We reanalyze by race, and the results showed that the rs11615 polymorphic loci were different for different races. Subgroup analyses of race point out that the correlation between the allele model and the dominant, recessive, homozygote genetic model of ERCC1 rs11615 gene polymorphism and the risk of CRC was statistically significant in Asians, but not in Caucasians. This is similar to the study of meta-analysis by Xie et al. which also pointed out a significant association between 19007 T > C polymorphism and risk of lung cancer in

Figure 3: Begg’s funnel plots of the association between ERCC1 rs11615 genetic polymorphism and CRC risk under different models. (a) Allele model (T vs. C). (b) Dominant model (TT + TC vs. CC). (c) Recessive model (TT vs. TC + CC). (d) Homozygote model (TT vs. CC).
Asians rather than Caucasians [37]. To note, it occurred differently between subgroups of Asians and Caucasians based on a study by Ding et al. of ERCC1 rs11615 and the risk of head and neck carcinomas as well [38]. We agreed to the suggestion that genetic backgrounds play their part. Some particular environmental exposures, habits, and customs modified the difference among diverse races [37]. Most of the single nucleotide polymorphisms are associated with other genetic polymorphisms and the environment. They regulate the genetic susceptibility of human disease, increase the likelihood of cancer occurrence, and accelerate malignant progression. Interestingly, these associations loss in brain tumors [39]. Li et al. have expounded that no evidence supported the association between cancer and ERCC1 rs11615 in 2007 [40]. To our regret, his study only conducted two articles on colorectal cancer and did not analyze CRC alone. ERCC1 rs11615 mutation has different correlations in different parts of the tumor, and there is a certain degree of disagreement even in the same tumor. Subgroup analyses of HWE and source of control indicated that heterogeneity was from the subgroup of HWE less than 0.05 and population-based studies. The outcomes of publication bias and sensitivity analysis have supported the reliability of this meta-analysis. Since 1990s, it was proved that repair of DNA damage may be suppressed in the case of high expression of ERCC1. This resulted in increased resistance of patients with platinum chemotherapeutic agents [41, 42]. Seetharam et al. got the same conclusion when they used siRNA to silence the ERCC1 in CRC cells and found that CRC cells are sensitive to oxaliplatin-induced apoptosis while ERCC1 gene was inhibited [43]. Expression levels of ERCC1 were an independent factor of overall survival in stage III and IV CRC patients receiving oxaliplatin-based chemotherapy [44, 45]. ERCC1 gene polymorphism is not only associated with tumor susceptibility but also with the efficacy of platinum drugs’ treatment in various tumors. Therefore, a combined analysis of ERCC1 and other predictors or prognostic factors is expected to guide the individual clinical diagnosis and treatment.

5. Conclusion

Among the nine studies we included, some limitations were discovered when we conducted this meta-analysis. First of all, the source of the case, such as classification of pathological diagnosis, and specific location of cancer was not entirely consistent or not mentioned. We need more messages like family history, exposure history of smoke and alcohol, age, and gender to obtain the adjusted OR. Moreover, detection techniques of disease and diagnostic criteria may also contribute a certain impact to these effects. Although we have collected all the relevant literature as far as possible, we may ignore some of the “gray literatures” such as conference articles, special reports, and so on. What is more, it may result in missing some published literature in other languages. Besides, this study only focused on the SNP loci on the ERCC1 rs11615, without considering other sites caused by the linkage disequilibrium, and further haplotype analysis was not taken into account. The factors given above may cause bias.

With those limitations in mind, our meta-analysis results indicated that ERCC1 rs11615 polymorphism carrying T variant had an association with colorectal cancer in Asians and are still credible. There is evidence to support a certain predictive effect of ERCC1 and tumor susceptibility. In the future, we need more well-designed and large sample size investigations to confirm the precise correlation between ERCC1 rs11615 polymorphism and CRC susceptibility.
Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Authors’ Contributions

Min Liu and Zhifeng Qiu are co-first author and contributed equally to this work.

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