Int J Clin Exp Med 2018;11(4):3043-3050
www.ijcem.com /ISSN:1940-5901/IJCEM0063709

Review Article

Associations between seven polymorphisms in ERCC5 and gastric cancer susceptibility: a systematic review and meta-analysis

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Received February 7, 2017; Accepted January 13, 2018; Epub April 15, 2018; Published April 30, 2018

Abstract: Accumulating evidences have highlighted the potential associations between ERCC5 genetic polymorphisms and gastric cancer susceptibility, however, inconclusive conclusions have yet been reached. Therefore, this meta-analysis was conducted to derive a more reliable conclusion of the relationship between ERCC5 genetic polymorphisms and gastric cancer risk. Thirteen eligible case-control studies were included in the present meta-analysis by using Electronic databases PubMed, Cochrane Library and Web of Science. The odds ratio with 95% confidence interval were calculated to evaluate the associations between ERCC5 genetic polymorphisms and gastric cancer susceptibility. Our study demonstrated rs751402 polymorphism in ERCC5 was related to an increased susceptibility to gastric cancer in all genetic models. Rs873601 polymorphism was conferred an increased susceptibility to gastric cancer in both allele model and recessive model. On the contrary, Rs1800975 polymorphism was related to a decreased susceptibility to gastric cancer in three genetic models (allele model: OR=0.702, 95% CI=0.532-0.925, P=0.012; homozygote model: OR=0.493, 95% CI=0.278-0.875, P=0.016 and recessive model: OR=0.628, 95% CI=0.416-0.947, P=0.027). Besides, a decreased susceptibility between gastric cancer and rs17655 polymorphism was identified only in recessive model. However, no significant association was observed between three (rs2094258, rs1047768 and rs2296147) polymorphisms and risk of gastric cancer in all genetic models. In Conclusion, our meta-analysis reveals that rs751402 and rs873601 polymorphism in ERCC5 may be risk factors for gastric cancer and rs1800975 and rs17655 polymorphism in ERCC5 may be protective factors. However, no significant association was observed between this other three polymorphisms and risk of gastric cancer.

Keywords: ERCC5, polymorphism, gastric cancer, meta-analysis

Introduction

Gastric cancer is one of most common malignancies worldwide, and its incidence and mortality has captured our great attention in past several decades [1]. There are many external risk factors of gastric cancer, such as cigarette smoking, obesity, helicobacter pylori infection, low intake of fresh fruits and vegetables [2]. But these external risk factors do not lead to gastric cancer; the inherent risk factors, like genetic susceptibility, may play vital roles in the susceptibility to gastric cancer [3]. Excision repair cross-complementing rodent repair deficiency, complementation group 5 (ERCC5), also known as Xeroderma pigmentosum complementation group G (XPG), one of nucleotide excision repair (NER) genes, is involved in DNA repair mechanism [4]. DNA repair genes play crucial roles in maintaining the stability and integrity of genomic DNA, including nucleotide excision repair (NER) genes [5]. Accumulating evidences demonstrated that genetic polymorphisms in the ERCC5 gene may contribute to the development of various cancers, such as breast cancer [6] and colorectal cancer [7]. Several studies have explored the correlation between ERCC5 genetic polymorphisms and gastric cancer susceptibility [8-20]; however, the results were inconsistent and inconclusive. Therefore, we conducted this meta-analysis to derive a more reliable conclusion of the rela-

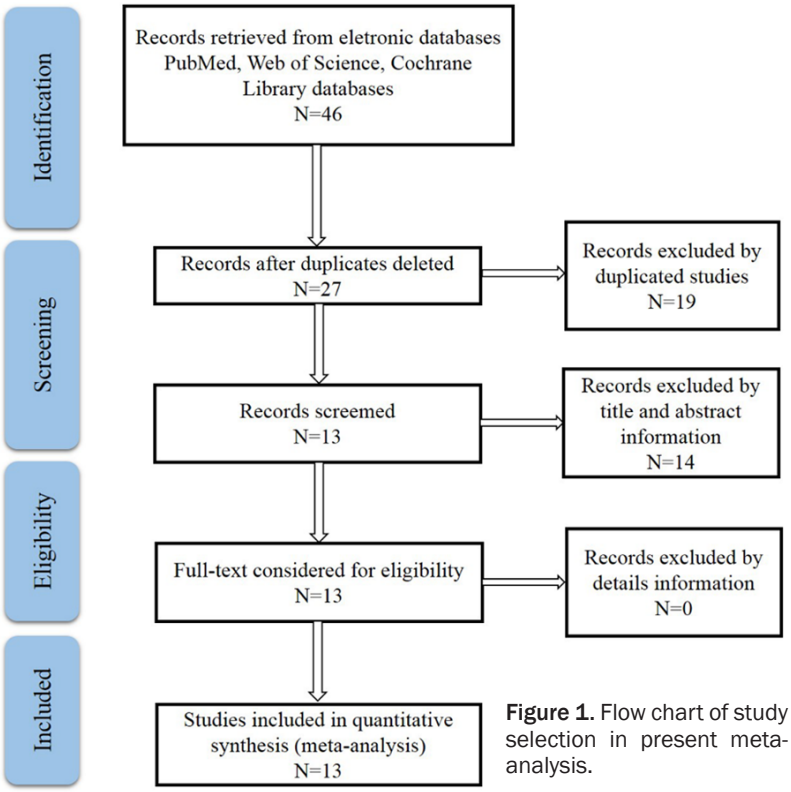

Figure 1. Flow chart of study selection in present meta-analysis.

tionship between ERCC5 genetic polymorphisms and gastric cancer risk.

Materials and methods

Search strategy

Electronic databases PubMed, Cochrane Library and Web of Science were performed by using ((Excision repair cross-complementing rodent repair deficiency, complementation group 5 OR ERCC5) OR (Xeroderma pigmentosum complementation group G OR XPG)) AND (polymorphism OR SNP OR variant OR mutation) AND (gastric cancer OR stomach cancer) as the keywords, in order to identify potentially relevant studies by 5 November, 2016. All eligible studies were checked carefully.

Inclusion and exclusion criteria

Potentially eligible studies were selected according to the following criteria: 1) Studies that evaluated the relationship between ERCC5 or XPG polymorphisms and gastric or stomach cancer susceptibility; 2) Only case-control studies; and 3) Studies included available data (allele and genotype frequencies) to calculate the crude ORs at 95% CIs. We excluded studies when they were 1) Case-only studies, reviews, case reports, meta-analysis, and comments; 2) Duplicate publications; and 3) Studies without available data of ERCC5 or XPG genotype.

Quality assessment

The quality of all eligible studies was evaluated independently by Si Huang and Anbang He on the basis of the Newcastle-Ottawa scale. Disagreements were settled with all investigators in conference (Supplementary Table 1).

Data extraction

Data extraction from the eligible studies were performed independently by four investigators (Si Huang, Anbang He, Depeng Xu and Qiwen Chen). The following information were extracted: the name of the first author, year of publication, ethnicity of each population, control source, genotyping method, total number of cases and controls, and *P*-value of HWE (Hardy-Weinberg equilibrium). Any disagreements were discussed with all investigators in conference until a consensus was reached.

Statistical analysis

All statistical analysis were carried out by STATA 12.0 software version (STATA Corp, College Station, TX, USA). Associations between the ERCC5 polymorphism and risk of gastric cancer were detected underlying genotyping models, including allele model, homozygote model, heterozygote model, recessive model and dominant model. The significance of the pooled ORs was evaluated by the Z test. HWE was detected by the Chi-square test among controls. Subgroup analysis was detected by source of controls, ethnicity, Genotyping method and HWE. The publication bias was tested by the Egger regression and Begg's funnel plots test. Between-study heterogeneity was evaluated by using the

Table 1. Characteristics of eligible studies in this meta-analysis

SNP	Reference	Year	Ethnicity	Genotyping method	Sample size (case/conctrol)	Source of control	Case			Control			HWE	Y/N
							BB	AB	AA	BB	AB	AA		
rs17655	Feng	2016	Asian	RFLP-PCR	177/237	PB	45	85	47	46	107	84	0.260	Y
rs17655	Canbay	2010	Caucasian	RFLP-PCR	40/247	PB	3	12	25	16	83	148	0.352	Y
rs17655	Bai	2016	Asian	RFLP-PCR	194/225	PB	73	100	21	94	112	19	0.072	Y
rs17655	Hussain	2009	Asian	SNPlex assay	173/370	PB	36	101	36	92	185	93	1.000	Y
rs17655	Guo	2016	Asian	RFLP-PCR	142/244	PB	56	76	10	118	114	12	0.018	N
rs17655	Li	2016	Asian	RFLP-PCR	216/216	HB	72	96	48	94	90	32	0.177	Y
rs2094258	Chen	2016	Asian	Taqman	692/771	HB	101	304	287	112	368	291	0.803	Y
rs2094258	Feng	2016	Asian	RFLP-PCR	177/238	PB	15	75	87	15	96	127	0.577	Y
rs2094258	He	2012	Asian	Taqman	1125/1196	PB	150	518	457	179	560	457	0.728	Y
rs2094258	Yang	2012	Asian	Taqman	337/347	HB	57	149	131	36	166	145	0.252	Y
rs2094258	Lu	2016	Asian	RFLP-PCR	184/206	PB	17	67	100	13	72	121	0.605	Y
rs2094258	Yang	2016	Asian	RFLP-PCR	155/246	HB	71	74	10	121	111	14	0.076	Y
rs751402	Chen	2016	Asian	Taqman	692/771	HB	93	313	286	89	331	351	0.416	Y
rs751402	Feng	2016	Asian	RFLP-PCR	177/236	PB	24	83	70	28	107	101	0.967	Y
rs751402	Li	2016	Asian	RFLP-PCR	216/216	HB	22	106	88	18	103	95	0.174	Y
rs751402	Lu	2016	Asian	RFLP-PCR	184/206	PB	24	91	69	22	97	87	0.510	Y
rs751402	Yang	2016	Asian	RFLP-PCR	155/246	HB	33	73	49	32	111	103	0.807	Y
rs751402	Duan	2012	Asian	RFLP-PCR	400/400	HB	47	181	172	29	165	206	0.605	Y
rs751402	Guo	2016	Asian	RFLP-PCR	142/274	PB	22	73	47	21	136	117	0.029	N
rs2296147	Chen	2016	Asian	Taqman	692/771	HB	33	217	442	32	264	475	0.535	Y
rs2296147	Duan	2012	Asian	RFLP-PCR	403/403	HB	24	122	257	11	132	260	0.232	Y
rs2296147	He	2012	Asian	Taqman	1125/1196	PB	54	371	700	56	398	742	0.779	Y
rs2296147	Yang	2012	Asian	Taqman	337/347	HB	24	105	208	41	110	196	0.000	N
rs873601	Chen	2016	Asian	Taqman	692/771	HB	187	333	172	170	396	205	0.415	Y
rs873601	He	2012	Asian	Taqman	1125/1196	PB	291	560	274	264	605	327	0.616	Y
rs873601	Yang	2012	Asian	Taqman	337/346	HB	78	163	96	91	164	91	0.333	Y
rs1047768	Li	2016	Asian	RFLP-PCR	216/216	HB	67	92	57	61	87	68	0.004	N
rs1047768	Hussain	2009	Asian	SNPlex assay	196/397	PB	13	71	112	28	175	194	0.173	Y
rs1800975	Bai	2016	Asian	RFLP-PCR	194/225	PB	55	98	41	87	106	32	0.975	Y

Notes: PHWE>0.05, polymorphisms conformed to HWE in the control group and PHWE≤0.05, polymorphisms did not conform to HWE in the control group. Abbreviations: SNP, single-nucleotide polymorphism; HWE, Hardy-Weinberg equilibrium; Y: P (HWE)>0.05; N: P (HWE)≤0.05; RFLP-PCR, restriction fragment length polymorphism-polymerase chain reaction; HB, hospital based; PB, population based.

Chi-square based Q test [21] and I^2 statistic [22]. No significant heterogeneity was observed when I^2<50% and P>0.10, and ORs were pooled by a fixed-effects model. Otherwise, the random-effects model was utilized. Sensitivity analyses were performed to assess the stability of the results. P<0.05 was considered as statistically significant.

Results

Included studies' identification and characteristics

As shown in **Figure 1**, a total of 46 studies were retrieved initially by the search strategy from database searches. After screening the title or abstract, we excluded 19 duplicated studies and 14 irrelevant studies. Next, 13 potential relevant studies were assessed by reading the full-length text. Finally, we collected 13 eligible studies that contain 29 case-control studies, including the seven polymorphisms in ERCC5 [8-20] (rs17655, rs2094258, rs751402, rs2296147, rs873601, rs1047768 and rs1800975) (**Table 1**).

Results of pooled meta-analysis

The results of rs751402 polymorphisms and gastric cancer risk were shown in **Table 2**, and the results of other polymorphisms were shown in **Table 3**. Overall, strongly significant association was found between the rs751402 polymorphism and risk of gastric cancer in all genetic models (allele model: OR=1.231, 95% CI=1.126-1.346, P=0.00 (**Figure 2**); homozygote model: OR=1.547, 95% CI=1.268-1.888, P=0.00; heterozygote model: OR=1.213, 95% CI=1.066-1.380, P=0.00; dominant model: OR=1.274,

Table 2. Results of meta-analysis for rs751402 polymorphisms in ERCC5 and gastric cancer susceptibility

Variables (rs751402)	Case/control	B vs A				BB vs AA			
		OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)
Total	1966/2349	1.231 (1.126, 1.346)	0.00	0.496	0	1.547 (1.268, 1.888)	0.00	0.391	4.7
Source of control									
PB	503/716	1.233 (1.042, 1.459)	0.015	0.40	0	1.596 (1.095, 2.327)	0.015	0.247	28.5
HB	1463/1633	1.230 (1.107, 1.367)	0.00	0.314	15.5	1.529 (1.209, 1.933)	0.00	0.327	13.2

BA vs AA				BB+BA vs AA				BB vs BA+AA			
OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)
1.213 (1.066, 1.380)	0.00	0.972	0	1.274 (1.127, 1.440)	0.00	0.801	0	1.401 (1.162, 1.689)	0.00	0.524	0
1.206 (0.942, 1.544)	0.14	0.845	0	1.273 (1.006, 1.612)	0.04	0.628	0	1.445 (1.016, 2.055)	0.04	0.296	17.8
1.216 (1.045, 1.415)	0.01	0.813	0	1.275 (1.104, 1.471)	0.00	0.545	0	1.385 (1.110, 1.726)	0.00	0.445	0

Notes: Fixed-model was used when *P*-value[a] for heterogeneity test ≥0.1; otherwise, random-effects model was used. Abbreviations: PB, Population Based; HB, Hospital Based; *P*-value[a]: *P*-values for heterogeneity from Q-test; OR, odds ratio; 95% CI, 95% confidence interval; n, number.

Table 3. Results of meta-analysis for six polymorphisms in ERCC5 and gastric cancer susceptibility

Variables (rs2094258)	Case/control	B vs A				BB vs AA			
		OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)
Total	2670/2735	0.983 (0.910, 1.062)	0.664	0.111	44.2	1.096 (0.830, 1.449)	0.517	0.077	49.8
Source of control									
PB	1486/1511	0.972 (0.875, 1.080)	0.598	0.126	51.7	1.098 (0.699, 1.724)	0.685	0.148	47.6
HB	1184/1224	0.996 (0.888, 1.118)	0.947	0.094	57.6	1.128 (0.697, 1.826)	0.623	0.068	62.8
Genotyping method									
RFLP-PCR	516/562	1.086 (0.906, 1.301)	0.373	0.368	63.9	1.276 (0.806, 2.021)	0.298	0.027	72.4
Taqman	2154/2173	0.961 (0.882, 1.047)	0.366	0.063	0	1.049 (0.724, 1.520)	0.8	0.492	0

BA vs AA				BB+BA vs AA				BB vs BA+AA			
OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)
0.938 (0.836, 1.053)	0.278	0.741	0	0.955 (0.856, 1.065)	0.41	0.412	0.7	1.089 (0.864, 1.373)	0.47	0.087	48
0.976 (0.839, 1.135)	0.754	0.509	0	0.971 (0.842, 1.121)	0.691	0.255	26.9	1.048 (0.733, 1.497)	0.8	0.234	31.2
0.887 (0.741, 1.061)	0.19	0.691	0	0.933 (0.787, 1.105)	0.419	0.338	7.8	1.132 (0.781, 1.643)	0.51	0.054	65.8
1.111 (0.841, 1.468)	0.459	0.916	0	1.154 (0.885, 1.504)	0.291	0.792	10	1.070 (0.755, 1.516)	0.71	0.33	9.8
0.906 (0.797, 1.028)	0.126	0.657	0	0.919 (0.815, 1.036)	0.167	0.329	0	1.104 (0.780, 1.561)	0.58	0.025	72.9

Variables	Case/control	B vs A				BB vs AA			
		OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)
rs17655(Total)	942/1539	0.919 (0.748, 1.128)	0.418	0.020	62.6	0.863 (0.562, 1.325)	0.501	0.04	57.1
rs873601 (Total)	2154/2313	1.103 (1.015, 1.198)	0.021	0.121	52.7	1.173 (0.907, 1.515)	0.224	0.117	53.5
rs2296147 (Total)	2557/2717	0.966 (0.880, 1.060)	0.466	0.156	42.5	1.039 (0.655, 1.648)	0.147	0.026	67.7
rs1047768 (Total)	412/613	0.970 (0.669, 1.406)	0.873	0.053	73.3	1.110 (0.744, 1.654)	0.61	0.263	20.2
rs1800975 (Total)	194/225	0.702 (0.532, 0.925)	0.012			0.493 (0.278, 0.875)	0.016		

BA vs AA				BB+BA vs AA				BB vs BA+AA			
OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)	OR (95%)	P	*P*-value[a]	I^2 (%)
1.063 (0.845, 1.339)	0.602	0.254	24.0	0.955 (0.687, 1.327)	0.782	0.067	51.4	0.826 (0.687, 0.994)	0.043	0.183	33.8
1.044 (0.906, 1.204)	0.553	0.694	0	1.097 (0.960, 1.254)	0.175	0.399	0	1.185 (1.033, 1.359)	0.02	0.107	55.3
0.939 (0.835, 1.055)	0.288	0.877	0	0.947 (0.847, 1.059)	0.341	0.596	0	1.065 (0.673, 1.683)	0.79	0.024	68.2
0.925 (0.522, 1.640)	0.79	0.049	74.1	0.947 (0.536, 1.672)	0.85	0.035	77.4	1.082 (0.761, 1.539)	0.66	0.624	0
0.722 (0.421, 1.235)	0.234			0.619 (0.372, 1.029)	0.064			0.628 (0.416, 0.947)	0.027		

Notes: Fixed-model was used when *P*-value[a] for heterogeneity test ≥0.1; Otherwise, random-effects model was used. Abbreviations: PB, Population Based; HB, Hospital Based; *P*-value[a]: *P*-values for heterogeneity from Q-test; OR, odds ratio; 95% CI, 95% confidence interval; n, number.

95% CI=1.127-1.440, P=0.00 and recessive model: OR=1.401, 95% CI=1.162-1.689, P=0.00). Rs873601 polymorphism was conferred an increased susceptibility to gastric cancer in

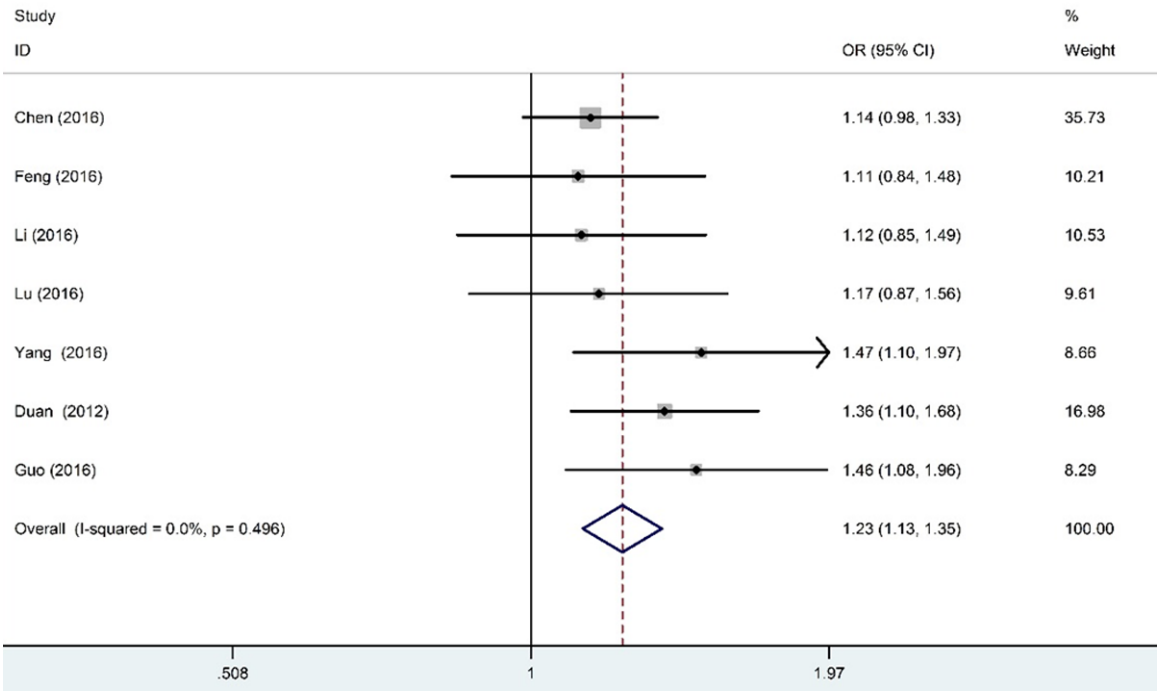

Figure 2. Forest plots of the relationship between rs751402 polymorphism in ERCC5 and gastric cancer risk in allele model (T vs C).

both allele model (OR=1.103, 95% CI=1.015-1.198, P=0.021) and recessive model (OR=1.185, 95% CI=1.033-1.359, P=0.020). On the contrary, Rs1800975 polymorphism was related to a decreased susceptibility to gastric cancer in three genetic models (allele model: OR=0.702, 95% CI=0.532-0.925, P=0.012; homozygote model: OR=0.493, 95% CI=0.278-0.875, P=0.016 and recessive model: OR=0.628, 95% CI=0.416-0.947, P=0.027). Besides, a decreased susceptibility between gastric cancer and rs17655 polymorphism was identified only in recessive model (OR=0.826, 95% CI=0.687-0.994, P=0.043). However, no significant association was observed between three (rs2094258, rs1047768 and rs2296147) polymorphisms and risk of gastric cancer in all genetic models (**Table 3**).

Result of subgroup

The results of subgroup analyses were showed in **Tables 2** and **3**. When the subgroup analysis was carried out by source of control, rs751402 polymorphism was related to an increased susceptibility to gastric cancer in all genetic models (**Table 2**). However, no significant association was found between rs2094258 polymorphism and risk of gastric cancer in all genetic models (**Table 3**). In the subgroup analysis of genotyping method, rs2094258 polymorphism was also conferred no significant susceptibility to gastric cancer in all genetic models (**Table 3**).

Sensitivity analysis and publication bias

Sensitivity analysis was used to evaluate the influence of individual case-control study on the pooled ORs by removing each study in turn and no significant influence on the pooled ORs was identified (Supplementary Table 2). Sensitivity analysis of the rs751402 polymorphism in the allele model is showed in **Figure 3** (Supplementary Table 2). Besides, both Begg's test and Egger's test were calculated to assess potential publication bias. The funnel plot of rs751402 polymorphism in the allele model was presented in **Figure 4** (Begg's test, P>|t|=0.230, Egger's test, P>|t|=0.436). According to Supplementary Table 3, no significant publication bias were observed.

Discussion

Nucleotide excision repair (NER), one of five major DNA repair pathways, contributes to maintaining the stability and integrity of genomic DNA in order to protect the genome from car-

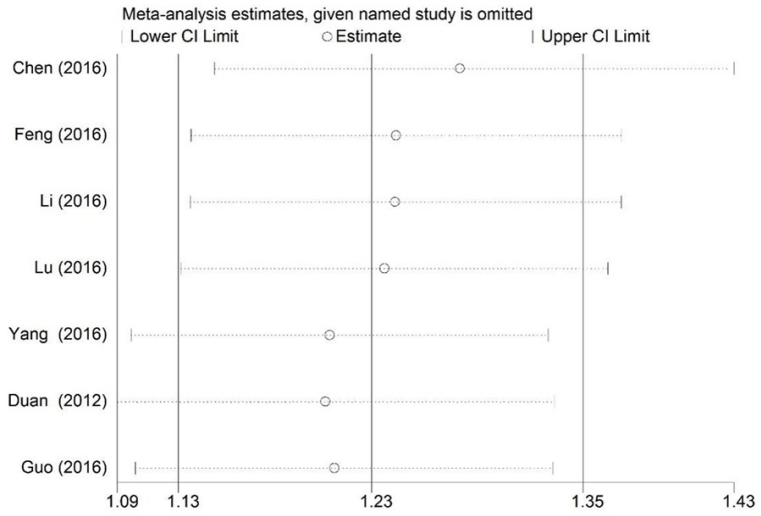

Figure 3. Sensitivity analysis of ERCC5 rs751402 polymorphism and gastric cancer risk in allele model (T vs C).

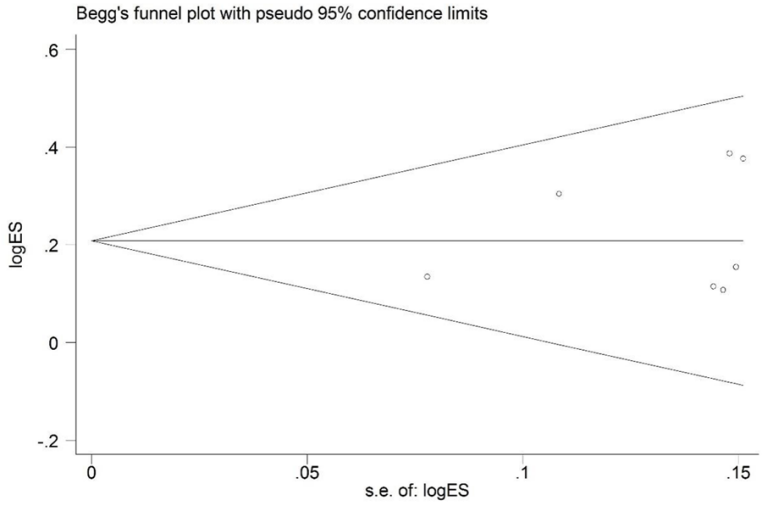

Figure 4. Begg's funnel plot for publication bias test under ERCC5 rs751402 polymorphism in allele model (T vs C).

cinogen-induced DNA damage [5]. ERCC5, as a structure-specific endonuclease, play a critical role in NER pathway, which is vital for amending the excision repair deficiency [23, 24]. Previous studies investigated association between seven polymorphisms in the ERCC5 gene and gastric cancer susceptibility. Lu et al [17] suggest that no significant association between two polymorphisms (rs2094258 and rs751402) in the ERCC5 gene and gastric cancer was identified. On the contrary, Duan et al [10] has found opposite results. The results still were controversial and inconsistent. Therefore, the present paper is the first meta-analysis to evaluate the association of seven polymorphisms in the ERCC5 gene with the risk of gastric cancer. As for rs2094258, rs1047768 and rs2296147, no significant associations were identified between three polymorphisms and risk of gastric cancer in all genetic models. However, rs751402 polymorphism was related to an increased susceptibility to gastric cancer in all genetic models (allele model: OR=1.231, 95% CI=1.126-1.346, P=0.00 (**Figure 2**); homozygote model: OR=1.547, 95% CI=1.268-1.888, P=0.00; heterozygote model: OR=1.213, 95% CI=1.066-1.380, P=0.00; dominant model: OR=1.274, 95% CI=1.127-1.440, P=0.00 and recessive model: OR=1.401, 95% CI=1.162-1.689, P=0.00). Moreover, Rs873601 polymorphism was conferred an increased susceptibility to gastric cancer in both allele model (OR=1.103, 95% CI=1.015-1.198, P=0.021) and recessive model (OR=1.185, 95% CI=1.033-1.359, P=0.020). On the contrary, Rs1800975 polymorphism was related to a decreased susceptibility to gastric cancer in three genetic models (allele model: OR=0.702, 95% CI=0.532-0.925, P=0.012; homozygote model: OR=0.493, 95% CI=0.278-0.875, P=0.016 and recessive model: OR=0.628, 95% CI=0.416-0.947, P=0.027). No significant between-study heterogeneity and publication bias were observed.

Although an extensive retrieve was conducted, some limitations still should be mentioned. First of all, all eligible studies were conducted only in the Asian and Caucasian populations. So, the results may merely be suitable for these two populations. Second, because of lack of original data, an assessment of gene-gene, gene-environment effects could not be conducted in present meta-analysis. Third, only published

English articles were included in this paper, which may lead to discrepant results. Fourth, the limited number of eligible studies may weakened the reliability of the results.

Conclusion

In all, our meta-analysis reveals that rs751402 and rs873601 polymorphism in ERCC5 may be risk factors for gastric cancer and rs1800975 and rs17655 polymorphism in ERCC5 may be protective factors for gastric cancer. However, as for rs2094258, rs1047768 and rs2296147, no significant association was observed between this three polymorphisms and risk of gastric cancer. Therefore, larger-size, population-based and well-designed studies are needed be conducted to verify association between the polymorphisms in ERCC5 and risk of gastric cancer in the near future.

Acknowledgements

This work was supported by the Project of the National Science Foundation of China (Grant No. 81401750), Guangdong Science Plan (No. 2014A020212038), and Shenzhen Science Plan (Nos. JCYJ20140418182819179, JCYJ-20150330102720122, JCYJ201404150930-52190 and cxzz201418182638764) and PhD Start-up Fund of Shenzhen University (No. 80-100036104).

Disclosure of conflict of interest

None.

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Supplementary Table 1. Methodological quality of the included studies according to the Newcastle-Ottawa scale

SNP	Reference	Year	Adequacy of case definition	Representativeness of the cases	Selection of controls	Definition of controls	Comparability cases/controls	Ascertainment of exposure	Same method of ascertainment	Nonresponse rate
rs17655	Feng	2016	*	*	*	*	**	*	*	*
	Canbay	2010	*	*	*	*	**	*	*	*
	Bai	2016	*	*	*	*	**	*	*	*
	Hussain	2009	*	*	*	*	**	*	*	*
	Guo	2016	*	*	*	*	**	*	*	*
	Li	2016	*	*	*	*	**	*	*	*
rs2094258	Chen	2016	*	*	*	NA	**	*	*	*
	Feng	2016	*	*	*	*	**	*	*	*
	He	2012	*	*	*	*	**	*	*	*
	Yang	2012	*	*	*	*	**	*	*	*
	Lu	2016	*	*	*	*	**	*	*	*
	Yang	2016	*	*	*	*	**	*	*	*
rs751402	Chen	2016	*	*	*	NA	**	*	*	*
	Feng	2016	*	*	*	*	**	*	*	*
	Li	2016	*	*	*	*	**	*	*	*
	Lu	2016	*	*	*	*	**	*	*	*
	Yang	2016	*	*	*	*	**	*	*	*
	Duan	2012	*	*	*	NA	**	*	*	*
	Guo	2016	*	*	*	*	**	*	*	*
rs2296147	Chen	2016	*	*	*	NA	**	*	*	*
	Duan	2012	*	*	*	NA	**	*	*	*
	He	2012	*	*	*	*	**	*	*	*
	Yang	2012	*	*	*	*	**	*	*	*
rs873601	Chen	2016	*	*	*	NA	**	*	*	*
	He	2012	*	*	*	*	**	*	*	*
	Yang	2012	*	*	*	*	**	*	*	*
rs1047768	Li	2016	*	*	*	*	**	*	*	*
	Hussain	2009	*	*	*	*	**	*	*	*
rs1800975	Bai	2016	*	*	*	*	**	*	*	*

Notes: This table identifies “high”-quality choices with a “*” A study can be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars can be given for comparability. Abbreviation: NA: Not Applicable.

Supplementary Table 2. Details of the sensitivity analyses for seven polymorphisms in ERCC5 and gastric cancer

SNP	Comparison	Study omitted	Estimate	Lower CI	Upper CI	Effect model
rs17655	C VS G	Feng (2016)	0.841	0.730	0.970	Random
		Canbay (2010)	0.915	0.727	1.150	
		Bai (2016)	0.930	0.721	1.200	
		Hussain (2009)	0.899	0.695	1.163	
		Guo (2016)	0.951	0.750	1.206	
		Li (2016)	0.982	0.803	1.200	
		Combined	0.919	0.748	1.128	
	CC VS GG	Feng (2016)	0.713	0.525	0.968	Random
		Canbay (2010)	0.842	0.524	1.352	
		Guo (2009)	0.898	0.536	1.504	
		Hussain (2009)	0.826	0.477	1.431	
		Li (2011)	0.919	0.569	1.484	
		Guo (2016)	1.006	0.668	1.517	
		Combined	0.863	0.562	1.325	
	CG VS GG	Feng (2016)	0.962	0.736	1.257	Fixed
		Canbay (2010)	1.089	0.854	1.388	
		Guo (2009)	1.102	0.863	1.409	
		Hussain (2009)	0.961	0.734	1.257	
		Li (2011)	1.085	0.855	1.377	
		Guo (2016)	1.169	0.904	1.511	
		Combined	1.063	0.845	1.339	
	CG+CC VS GG	Feng (2016)	0.852	0.625	1.161	Random
		Canbay (2010)	0.956	0.649	1.407	
		Guo (2009)	0.987	0.677	1.439	
		Hussain (2009)	0.878	0.591	1.304	
		Li (2011)	0.989	0.690	1.417	
		Guo (2016)	1.102	0.822	1.477	
		Combined	0.955	0.687	1.327	
	CC VS CG+GG	Feng (2016)	0.748	0.611	0.915	Fixed
		Canbay (2010)	0.820	0.681	0.989	
		Guo (2009)	0.822	0.667	1.014	
		Hussain (2009)	0.834	0.680	1.022	
		Li (2011)	0.861	0.701	1.058	
		Guo (2016)	0.886	0.718	1.092	
		Combined	0.826	0.687	0.994	
rs751402	T VS C	Chen (2016)	1.279	1.145	1.429	Fixed
		Feng (2016)	1.244	1.132	1.367	
		Li (2016)	1.244	1.132	1.367	
		Lu (2016)	1.238	1.127	1.360	
		Yang (2016)	1.208	1.100	1.327	
		Duan (2012)	1.206	1.092	1.331	
		Guo (2016)	1.211	1.102	1.330	
		Combined	1.231	1.126	1.346	
	TT VS CC	Chen (2016)	1.725	1.343	2.215	Fixed
		Feng (2016)	1.587	1.286	1.958	
		Li (2016)	1.570	1.275	1.933	

		Lu (2016)	1.566	1.270	1.930	
		Yang (2016)	1.483	1.201	1.833	
		Duan (2012)	1.482	1.193	1.841	
		Guo (2016)	1.478	1.200	1.820	
		Combined	1.547	1.268	1.888	
	TC VS CC	Chen (2016)	1.242	1.059	1.456	Fixed
		Feng (2016)	1.223	1.068	1.401	
		Li (2016)	1.226	1.070	1.405	
		Lu (2016)	1.216	1.062	1.393	
		Yang (2016)	1.199	1.048	1.372	
		Duan (2012)	1.190	1.031	1.374	
		Guo (2016)	1.202	1.051	1.376	
		Combined	1.213	1.066	1.380	
	TT+TC VS CC	Chen (2016)	1.324	1.137	1.541	Fixed
		Feng (2016)	1.289	1.133	1.466	
		Li (2016)	1.290	1.134	1.468	
		Lu (2016)	1.280	1.126	1.455	
		Yang (2016)	1.251	1.100	1.421	
		Duan (2012)	1.244	1.086	1.426	
		Guo (2016)	1.255	1.104	1.426	
		Combined	1.274	1.127	1.440	
	TT VS TC+CC	Chen (2016)	1.539	1.217	1.945	Fixed
		Feng (2016)	1.431	1.175	1.744	
		Li (2016)	1.416	1.165	1.721	
		Lu (2016)	1.417	1.165	1.724	
		Yang (2016)	1.353	1.109	1.652	
		Duan (2012)	1.353	1.104	1.657	
		Guo (2016)	1.345	1.106	1.635	
		Combined	1.401	1.162	1.689	
rs2094258	T VS C	Chen (2016)	1.005	0.918	1.100	Fixed
		Feng (2016)	0.971	0.896	1.052	
		He (2012)	1.034	0.934	1.146	
		Yang (2012)	0.953	0.877	1.035	
		Lu (2016)	0.970	0.896	1.051	
		Yang (2016)	0.988	0.912	1.071	
		Combined	0.983	0.910	1.062	
	TT VS CC	Chen (2016)	1.195	0.810	1.763	Random
		Feng (2016)	1.066	0.788	1.442	
		He (2012)	1.223	0.878	1.706	
		Yang (2012)	0.921	0.768	1.104	
		Lu (2016)	1.054	0.786	1.413	
		Yang (2016)	1.138	0.834	1.553	
		Combined	1.096	0.830	1.449	
	TC VS CC	Chen (2016)	0.978	0.854	1.120	Fixed
		Feng (2016)	0.922	0.817	1.040	
		He (2012)	0.948	0.813	1.105	
		Yang (2012)	0.930	0.822	1.053	
		Lu (2016)	0.924	0.820	1.042	
		Yang (2016)	0.938	0.835	1.054	

	Combined	0.938	0.836	1.053	
TT+TC VS CC	Chen (2016)	0.995	0.875	1.131	Fixed
	Feng (2016)	0.938	0.837	1.051	
	He (2012)	0.996	0.861	1.151	
	Yang (2012)	0.932	0.829	1.048	
	Lu (2016)	0.938	0.837	1.051	
	Yang (2016)	0.957	0.857	1.068	
	Combined	0.955	0.856	1.065	
TT VS TC+CC	Chen (2016)	1.146	0.835	1.574	Random
	Feng (2016)	1.073	0.834	1.379	
	He (2012)	1.185	0.900	1.561	
	Yang (2012)	0.953	0.813	1.117	
	Lu (2016)	1.062	0.831	1.356	
	Yang (2016)	1.158	0.876	1.532	
	Combined	1.089	0.864	1.373	

Supplementary Table 3. *P*-values of the Begg's test and Egger's test for three polymorphisms (rs2094258, rs751402 and rs17655) in ERCC5 in the allele model

Polymorphism	Subgroup	Begg's test P>|t|	Egger's test P>|t|
rs2094258	Overall	0.260	0.136
rs751402	Overall	0.230	0.436
rs17655	Overall	1.000	0.912