ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2019 September 14; 25(34): 5017-5219

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 25 Number 34 September 14, 2019

World Journal of Gastroenterology
Volume 25 Number 34 September 14, 2019

Contents

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

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PUBLICATION DATE
September 14, 2019

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World Journal of Gastroenterology

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World J Gastroenterol 2019 September 14; 25(34): 5152-5161

DOI: 10.3748/wjg.v25.i34.5152

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Case Control Study

Association of *XPG* rs2094258 polymorphism with gastric cancer prognosis

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Author contributions: Wang XQ wrote the manuscript; Wang XQ and Terry PD analyzed the data; Li Y, Zhang Y, and Kou WJ performed the majority of experiments; Wang XQ and Wang MX designed the research; Wang MX and Terry PD revised the manuscript.

Supported by the Fundamental Research Funds for the Central Universities, No. zdyf2017007.

Institutional review board statement: This study was approved by the Institutional Review Board of Health Science Center of Xi'an Jiaotong University.

Informed consent statement: Informed consent was obtained from all study participants.

Conflict-of-interest statement: The authors declare no conflict of interest.

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Abstract

BACKGROUND

The xeroderma pigmentosum group G (*XPG*) gene at chromosome 13q33 consists of 15 exons, which may be related to the occurrence and development of gastric cancer (GC).

AIM

To examine the association of several common single nucleotide polymorphisms (SNPs) of the *XPG* gene with GC risk and survival.

METHODS

Five SNPs of *XPG* (rs2094258, rs751402, rs873601, rs2296147, and rs1047768) were genotyped by PCR restriction fragment length polymorphism in 956 histologically confirmed GC cases and 1012 controls in North China. GC patients were followed for survival status and, if deceased, cause of death. Logistic regression and Cox regression were used for analysing associations of *XPG* SNPs with risk of GC and prognosis, respectively. For rs2094258, heterozygous model (CT *vs* CC), homozygous model (TT *vs* CC), recessive model (TT *vs* CT + CC), and dominant model (TT + CT *vs* CC) were analyzed.

RESULTS

None of the examined loci were statistically associated with GC risk, although rs2296147 was marginally associated with GC risk ($P = 0.050$). GC patients with the rs2094258 CT + CC genotype showed worse survival than those with the TT genotype (log-rank test, $P = 0.028$), and patients with the CC genotype had a tendency of unfavourable prognosis compared with those with the TT + CT genotype (log-rank test, $P = 0.039$). The increase in C alleles of rs2094258 [hazard

Manuscript source: Unsolicited manuscript

Received: May 16, 2019
Peer-review started: May 16, 2019
First decision: July 21, 2019
Revised: July 25, 2019
Accepted: August 19, 2019
Article in press: August 19, 2019
Published online: September 14, 2019

P-Reviewer: Can G, Virgilio E
S-Editor: Yan JP
L-Editor: Wang TQ
E-Editor: Zhang YL

ratio (HR) = 1.19, 95% confidence interval (CI): 1.02-1.45, P = 0.037] were associated with the long-term survival of GC cases. Other risk factors for survival included tumor differentiation (HR = 4.51, 95%CI: 1.99-8.23, P < 0.001), lymphovascular invasion (HR = 1.97, 95%CI: 1.44-3.01, P < 0.001), and use of chemotherapy (HR = 0.81, 95%CI: 0.63-0.98, P = 0.041).

CONCLUSION
The *XPG* rs2094258 polymorphism may be associated with overall survival in GC patients.

Key words: Xeroderma pigmentosum group G; Single nucleotide polymorphisms; rs2094258; Gastric cancer; Prognosis

Core tip: This study investigated the relationships between five functional single nucleotide polymorphisms of the xeroderma pigmentosum group G (*XPG*) (rs2094258, rs751402, rs2296147, rs1047768, and rs873601) and gastric cancer (GC) risk and survival. The results showed an association between the *XPG* rs2094258 polymorphism and overall survival in patients with GC. GC patients with the rs2094258 CT + CC genotype showed a worse survival than those with the TT genotype, and patients with the CC genotype had a tendency of unfavourable prognosis compared with those with the TT + CT genotype. The increase in the number of C alleles of rs2094258 was associated with the long-term survival of GC cases.

Citation: Wang XQ, Terry PD, Li Y, Zhang Y, Kou WJ, Wang MX. Association of *XPG* rs2094258 polymorphism with gastric cancer prognosis. *World J Gastroenterol* 2019; 25(34): 5152-5161
URL: https://www.wjgnet.com/1007-9327/full/v25/i34/5152.htm
DOI: https://dx.doi.org/10.3748/wjg.v25.i34.5152

INTRODUCTION

Gastric cancer (GC) is one of the global leading causes of cancer-related death[1]. The World Health Organization (WHO) estimates that 1.03 million people are diagnosed and 783000 die of the disease each year[2]. The highest age standard incidence per 100000 population is observed in Eastern Asia[3], especially in China, at 22.7 per 100000[4]. Multiple factors contribute to the development of this disease, including environmental and genetic factors, such as *Helicobacter pylori* (*H. pylori*) infection, drinking, obesity, a high-salt diet, and various genetic factors[5]. Although GC morbidity and mortality have declined in recent years, the social and economic burden of the disease remains high[1,6,7].

DNA repair genes play a key role in maintaining the genomic DNA stability and integrity. Functional genetic variants of DNA repair genes may change the host DNA repair ability and thus affect tumor prognosis[8]. DNA repair genes participate in many crucial pathways including nucleotide excision repair (NER), which is involved in the repair of some types of DNA damage. Recent evidence suggests that NER factors function in processes that facilitate mRNA synthesis or shape three-dimensional chromatin structure[9]. Xeroderma pigmentosum group G (XPG or ERCC5) plays a key role in NER repair, as it can recognize DNA damage and initiate the NER process[10]. XPG has 3′-junction cutting ability on bubble substrates, resulting in 3′-incision in the human double-incision) repair system, and non-catalytically XPG is needed for subsequent 5′-incision by XPF-ERCC1[11].

Some studies have demonstrated that the single nucleotide polymorphisms (SNPs) of *XPG* may affect the development of cancer, such as lung cancer[12,13], colorectal cancer[14,15], breast cancer[16], neuroblastoma[17], Hodgkin's lymphoma[18], and oral squamous cell carcinoma[19]. However, only a few studies have explored the associations between *XPG* gene SNPs and GC, and those studies show inconsistent results. Some studies reported no associations[20-22], while others demonstrated varying degrees of association[23,24]. Furthermore, few studies have explored the potential prognostic importance of *XPG* SNPs in GC patients[25]. Therefore, we examined GC

risk and survival in relation to common functional *XPG* SNPs in a case-control study in North China.

MATERIALS AND METHODS

Study subjects

From September 2010 to June 2013, pathologically confirmed incident GC cases were selected from the First Affiliated Hospital of Xi'an Jiaotong University. During the same time period, controls were recruited from the Physical Examination Centre of the First Affiliated Hospital of Xi'an Jiaotong University. The cases and controls were matched by sex, age (within 5 years), and residential district. Socio-demographic and clinical data were collected during recruitment, such as alcohol consumption and smoking status. TNM staging of GC tumors was done according to the WHO standard. *H. pylori* infection status was tested by ELISA. The present study protocol was approved by the Institutional Review Board of Health Science Center of Xi'an Jiaotong University. Informed consent was obtained from all study participants.

Follow-up

Cases were followed for survival status and chemotherapy data every 3 mo within the first year and then annually afterwards. Causes and dates of death were recorded, and survival time was calculated from the date of recruitment. Survival time was calculated from time of recruitment to date of death, date of last contact (for those lost to follow-up), or to the last contact with living subjects at the end of the study.

Genotyping

Peripheral blood samples from all cases and controls were collected by the investigators. The TIANamp Blood DNA Kit (Tiangen, Beijing, China) was used for DNA extraction. XPG rs2094258, rs751402, rs873601, rs2296147, and rs1047768 polymorphism genotyping was performed by PCR restriction fragment length polymorphism (PCR-RFLP). The conditions of PCR amplification were: (1) Denaturation at 95 °C for 5 min; (2) 30 cycles of denaturation at 94 °C for 60 s, annealing at 60 °C for 60 s, and extension at 72 °C for 60 s; and (3) Extension at 72 °C for 10 min. PCR products were confirmed by agarose gel electrophoresis. Ten percent of the samples were randomly selected for repeated genotyping and the results were 100 percent consistent.

Statistical analysis

The socio-demographic data and clinical data between case and control subjects were compared by the chi-square test. A goodness-of-fit chi-squared test was also used to analyze whether the SNP (XPG rs2094258, rs751402, rs2296147, rs1047768 and rs873601) distributions conform to the Hardy-Weinberg equilibrium (HWE) in controls. Odds ratios (ORs) and 95% confidence intervals (CIs) for examined SNPs were analyzed by Logistic regression method and adjusted by age, gender, and *H. pylori* infection status. The heterozygous model, homozygous model, recessive model, and dominant model were all analyzed for five SNPs. For rs2094258, heterozygous model, homozygous model, recessive model, and dominant model were CT *vs* CC, TT *vs* CC, TT *vs* CT + CC, TT + CT *vs* CC, respectively. Kaplan-Meier method and log-rank test were used for plotting cases' survival curves and for comparisons, respectively.

Multivariate Cox regression was used for exploring possible prognostic factors, which included gender, age, drinking, smoking, *H. pylori*, TNM stage, tumor differentiation, lymphovascular invasion, neural invasion, and chemotherapy. SPSS 24.0 statistical software was used for all statistical analyses (Statistical Package for the Social Sciences, version 24, SSPS Inc, Chicago, IL, United States). All statistical tests were two-sided, with $P < 0.05$ as the boundary value.

RESULTS

The majority of study participants were male and less than age 60, with no significant differences in these factors between cases and controls (Table 1). All five loci in the control group were consistent with the Hardy-Weinberg equilibrium. The rate of *H. pylori* infection in GC patients was significantly higher than that in the control group (70.6% *vs* 53.6%, $P < 0.001$). None of the associations between studied loci (rs2094258, rs751402, rs2296147, rs1047768, and rs873601) and GC risk was statistically significant (Table 2). However, the rs2296147 CC genotype frequency was higher in the GC case

group than that in the control group (5.9% *vs* 3.9%, $P = 0.050$). After adjustment for age, sex, and *H. pylori* status, this genotype was marginally associated with a slightly higher risk of GC (OR = 1.40, 95%CI: 0.97-2.50, $P = 0.061$) than the TT genotype. The CC genotype was found to be marginally associated with a higher risk of GC (OR = 1.36, 95%CI = 0.99-2.49, $P = 0.053$) in the recessive model (CC *vs* CT + TT).

As the number of C alleles of rs2094258 increased, the survival rate of GC cases decreased (log-rank test, $P = 0.032$) (Table 3). Among all the cases, mortality was 45.4% with rs2094258 TT genotype (no C allele), 53.7% with CT genotype (one C allele), and 59.4% with CC genotype (two C alleles). The other four SNP loci (rs751402, Rs2296147, rs1047768, and rs873601) had no significant correlation with overall survival in patients with GC. For rs2094258, survival curves varied significantly with genotype (log-rank test, $P = 0.032$) (Figure 1A). GC patients with the rs2094258 CT + CC genotype showed a lower survival than patients with the TT genotype (log-rank test, $P = 0.028$) (Figure 1B). Cases with the CC genotype had a poorer prognosis than those with the TT + CT genotype (log-rank test, $P = 0.039$) (Figure 1C).

In univariate survival analysis, age ($P = 0.011$), TNM stage ($P < 0.001$), no chemotherapy ($P < 0.001$), poor differentiation ($P < 0.001$), neural invasion ($P < 0.001$), and lymphovascular invasion ($P < 0.001$) were positively associated with the 5-year survival of GC cases (Table 4). Gender and *H. pylori* status were not significantly associated with the 5-year survival of GC cases. In multivariate analysis, the increase in the number of C alleles of rs2094258 (hazard ratio [HR] = 1.19, 95%CI: 1.02-1.45, $P = 0.037$), chemotherapy (HR = 0.81, 95%CI: 0.63-0.98; $P = 0.041$), differentiation (HR = 4.51, 95%CI: 1.99-8.23, $P < 0.001$), and lymphovascular invasion (HR = 1.97, 95%CI: 1.44-3.01, $P < 0.001$) were associated with survival in GC cases (Table 5).

DISCUSSION

We genotyped five functional SNPs in the *XPG* gene involved in the NER pathway and assessed their associations with GC risk and survival in China. Although rs2296147 was marginally associated with risk of GC ($P = 0.05$), we found no statistically significant associations. However, as the number of C alleles of rs2094258 increased, the survival of GC cases showed a decreasing trend. Poor differentiation, lymphovascular invasion, no chemotherapy, and increase in the number of C alleles of rs2094258 were associated with decreased survival among cases.

Few studies have explored the association of *XPG* SNPs with survival in GC patients. Our results are similar to those of Liu *et al*[25], who analysed the association between *XPG* SNPs and survival among 373 GC patients in China. That study found that in univariate model, the survival rate of those with the *XPG* rs2094258 AG genotype was higher than that of wild-type GG carriers (HR = 0.59, 95%CI: 0.39-0.90, $P = 0.014$), and that in multivariate analysis, the AA + AG genotype presented a significant survival advantage over the GG genotype (adjusted HR = 0.65, 95%CI: 0.44-0.97)[25]. Liu *et al*[25] also found that the AA + AG genotype of the *XPG* rs2094258 polymorphism improved survival in those with the following characteristics: Age more than 60, lymphatic metastasis, TNM stage III-IV, Borrmann III–IV, and diffuse-type gastric tumors[25].

Consistent with our study, a recent meta-analysis did not observe an overall association between the *XPG* rs2094258 SNPs and GC risk[26]. Some studies have found associations between the rs2094258 polymorphism and GC risk[22,26-28]. For example, Yang *et al*[23] assessed three *XPG* SNPs (rs2296147T>C, rs2094258C>T, and rs873601G>A) and found that the rs2094258 C>T polymorphism was associated with an increased GC risk. Meanwhile, *H. pylori*-infected individuals with the rs2094258 TT genotype had a much higher GC risk (OR = 2.13, 95%CI: 1.22-3.35, P for interaction = 0.030)[23]. However, *H. pylori* status did not modify associations with this SNP in our data. Varying cofactors among study populations, small sample size, the use of different PCR methods, or the low penetrance of this SNP may account for the inconsistent findings[15].

XPG rs2296147 was not associated with GC in the present study, a finding consistent with those of other studies[24,25]. However, significant associations between rs2296147 polymorphisms and GC risk were observed in Asian populations in numerous studies in one meta-analysis (CT *vs* TT: OR = 0.93, 95%CI: 0.87-0.99, $P = 0.036$)[29]. Further, the rs2296147 CC genotype was associated with a reduced risk of GC in a Chinese population (OR = 0.52, 95%CI: 0.27-0.97)[23]. These differences may be due to regional differences, small sample size, or heterogeneity of clinical feature[26].

The NER pathway belongs to the DNA repair pathways, and its functions include removing exogenous or endogenous DNA damage or adduct between chains and recruiting proliferating-cell nuclear antigen to the damage site for the subsequent gap-

Table 1 Demographic characteristics of the participants

		Case	Control	X^2	*P*-value
		n = 956	*n* = 1012		
Age (yr)					
	≤60	569 (59.5)	637 (62.9)	2.289	0.130
	>60	387 (40.5)	375 (37.1)		
Gender					
	Male	667 (69.8)	724 (71.5)	0.662	0.416
	Female	289 (30.2)	288 (28.5)		
H. pylori infection					
	Positive	675 (70.6)	542 (53.6)	59.835	<0.001
	Negative	281 (29.4)	470 (46.4)		
Drinking					
	No	758 (79.3)	497 (49.1)	2.787	0.095
	Yes	198 (20.7)	515 (50.9)		
Smoking					
	No	560 (58.6)	517 (51.1)	1.382	0.240
	Yes	396 (41.4)	495 (48.9)		

H. pylori: *Helicobacter pylori*.

filling DNA synthesis[30]. DNA repair usually includes two stages of excision and repair synthesis[31]. The *XPG* gene locating at chromosome 13q33 consists of 15 exons[10], which is considered to cut the DNA at the 3′ terminus, initiate transcription-coupled DNA repair, and participate in RNA polymerase II transcription[32]. In the process of DNA repair, XPG binds to XPB as part of the transcription factor IIH (TFIIH) complex and strongly interacts with the TFIIH complex, a multi-subunit complex located at the intersection of transcription and DNA repair[33], which is involved in the DNA demethylation induced by overexpression of Gadd45a[10]. Meanwhile, XPG-related nucleases are used hierarchically for the excision of double-stranded rDNA break resection[34]. Recent report suggests that XPG incises the R-loop structure and participates in the RAD52-dependent resolution of DNA-RNA hybrids[35]. The rs1047768, rs751402, and rs2296147 are located in the exon 2, proximal promoter, and 5' untranslated region of the gene, respectively[36,37]. Based on the dbSNP database, the rs2094258 located at the *XPG* gene intron region participates in the initiation of the transcription-coupled DNA repair.

The limitations of this study are as follows. First, we could not explore and determine the exact mechanism by which *XPG* SNPs influence GC survival. Second, this study only examined five functional SNPs and did not include all the SNPs in the *XPG* gene that might play a key role in GC development. Third, selection bias and information bias are inherent threats to case-control studies, and cannot be ruled out in our study. Genetic factors have been shown to play key roles in the development, progression, and prognosis of GC. If confirmed by other studies, the results of our study suggest that *XPG* rs2094258 polymorphisms may serve as genetic biomarkers for GC prognosis, and may provide clues to biological underpinnings of GC progression.

Table 2 Single nucleotide polymorphism and genotype distribution between gastric cancer cases and controls

SNP	Genotype	Case	Control	HWE	*P*-value	OR	95%CI	*P*-value	OR[1]	95%CI	*P*-value
		n = 956	*n* = 1012								
Rs2094258	CC	390 (40.8)	437 (43.2)	0.318	0.853	1.00					
	CT	441 (46.1)	464 (45.8)			1.07	0.88-1.29	0.545	1.05	0.86-1.31	0.626
	TT	125 (13.1)	111 (11.0)			1.26	0.94-1.69	0.133	1.19	0.90-1.20	0.249
	Dominant	566 (59.2)	575 (56.8)			1.10	0.92-1.32	0.284	1.06	0.87-1.37	0.388
	Recessive	831 (86.9)	901 (89.0)			1.22	0.93-1.60	0.150	1.19	0.91-1.72	0.303
Rs751402	CC	366 (38.3)	371 (36.7)	0.183	0.913	1.00					
	CT	467 (48.8)	476 (47.0)			0.95	0.78-1.16	0.618	0.98	0.77-1.33	0.774
	TT	123 (12.9)	165 (16.3)			0.88	0.67-1.15	0.341	0.90	0.61-1.28	0.491
	Dominant	590 (61.7)	632 (62.5)			0.95	0.79-1.14	0.554	0.95	0.78-1.22	0.711
	Recessive	833 (87.1)	847 (83.7)			0.90	0.71-1.15	0.411	0.93	0.69-1.18	0.487
Rs2296147	TT	599 (62.7)	640 (63.2)	0.076	0.963	1.00					
	CT	301 (31.5)	332 (32.9)			0.97	0.80-1.17	0.745	0.97	0.80-1.19	0.674
	CC	56 (5.9)	40 (3.9)			1.50	0.98-2.28	0.059	1.40	0.97-2.50	0.061
	Dominant	357 (37.3)	372 (36.8)			1.03	0.85-1.23	0.789	1.01	0.80-1.38	0.865
	Recessive	900 (94.1)	973 (96.1)			1.51	1.00-2.29	0.050	1.36	0.99-2.49	0.053
Rs1047768	TT	505 (52.8)	540 (53.4)	0.367	0.832	1.00					
	CT	379 (39.6)	406 (40.1)			1.00	0.83-1.20	0.985	1.00	0.80-1.28	0.989
	CC	72 (7.6)	66 (6.5)			1.17	0.82-1.66	0.395	1.11	0.79-1.92	0.505
	Dominant	451 (47.2)	472 (46.6)			1.02	0.86-1.22	0.812	1.01	0.81-1.45	0.897
	Recessive	884 (92.5)	946 (93.5)			1.17	0.83-1.65	0.381	1.12	0.74-1.84	0.561
Rs873601	GG	271 (28.3)	288 (28.5)	0.247	0.884	1.00					
	AG	475 (49.7)	514 (50.8)			0.98	0.80-1.21	0.865	0.99	0.63-1.88	0.931
	AA	210 (22.0)	210 (20.7)			1.06	0.83-1.37	0.638	1.03	0.71-2.01	0.807
	Dominant	685 (71.7)	724 (71.5)			1.12	0.92-1.37	0.245	1.07	0.82-1.94	0.466
	Recessive	746 (78.0)	802 (79.2)			1.08	0.87-1.33	0.511	0.98	0.88-1.37	0.685

[1]OR was calculated by Logistic regression method after adjusting for age and gender. *H. pylori*: *Helicobacter pylori* infection status; SNP: Single nucleotide polymorphism; HWE: Hardy-Weinberg equilibrium; OR: Odds ratio.

Table 3 Genotypes of single nucleotide polymorphism and 5-year survival status of gastric cancer cases

SNP	Genotype	Case	Death (%)	5-yr survival rate (%)	*P*-value[1]
Rs2094258	CC	388	157 (40.5)	59.4	0.032
	CT	440	203 (46.1)	53.7	
	TT	123	68 (55.3)	45.4	
Rs751402	CC	363	162 (44.6)	55.3	0.523
	CT	465	216 (46.5)	53.3	
	TT	121	50 (41.3)	58.9	
Rs2296147	TT	589	281 (47.7)	52.0	0.217
	CT	297	124 (41.8)	57.6	
	CC	50	23 (46.0)	57.7	
Rs1047768	TT	501	243 (48.5)	51.2	0.102
	CT	375	152 (40.5)	59.1	
	CC	67	33 (49.3)	53.4	
Rs873601	GG	268	131 (48.9)	51.2	0.362
	AG	472	203 (43.0)	56.8	
	AA	207	94 (45.4)	54.7	

[1]*P* was calculated by log-rank test. SNP: Single nucleotide polymorphism.

Table 4 Univariate analysis of associations between influencing factors and 5-year survival of gastric cancer cases

Variable	Classification	*n*	Death (%)	5-yr survival rate (%)	*P*-value[1]
Gender	Male	667	303 (45.4)	54.2	0.399
	Female	289	125 (43.3)	56.1	
Age (yr)	≤60	569	235 (41.3)	58.5	0.011
	>60	387	193 (49.9)	49.7	
Drinking	No	758	335 (44.2)	55.6	0.259
	Yes	198	93 (47.0)	52.9	
Smoking	No	560	244 (43.6)	55.9	0.417
	Yes	396	184 (46.5)	53.3	
H. pylori infection	Negative	281	118 (42.0)	58.1	0.284
	Positive	675	310 (45.9)	51.4	
TNM stage	I	178	18 (10.1)	87.7	<0.001
	II	366	129 (35.2)	66.9	
	III	404	281 (69.6)	29.8	
Differentiation	Poor	661	329 (49.8)	50.0	<0.001
	Moderate or high	280	99 (35.4)	66.7	
Lymphovascular invasion	Negative	269	57 (21.2)	79.6	<0.001
	Positive	675	371 (55.0)	44.8	
Neural invasion	Negative	396	132 (33.3)	67.4	<0.001
	Positive	548	296 (54.0)	45.7	
Chemotherapy	No	361	281 (77.8)	22.9	<0.001
	Yes	592	147 (24.8)	75.1	

Missing values: 8 for tumor–node–metastasis stage, 15 for differentiation, 12 for lymphovascular invasion and neural invasion, and 3 for chemotherapy.
[1]*P* was calculated by log-rank test. *H. pylori*: *Helicobacter pylori*; TNM: Tumor–node–metastasis.

Table 5 Multivariate analysis of gastric cancer survival

Variable	Comparison	HR[1]	95%CI	*P*-value
Differentiation	Poor *vs* Moderate or high	4.51	1.99-8.23	<0.001
Lymphovascular invasion	Positive *vs* Negative	1.97	1.44-3.01	<0.001
Chemotherapy	Yes *vs* No	0.81	0.63-0.98	0.041
Rs2094258	Increase in C allele	1.19	1.02-1.45	0.037

[1]HR was calculated by Cox regression model. HR: Hazard ratio.

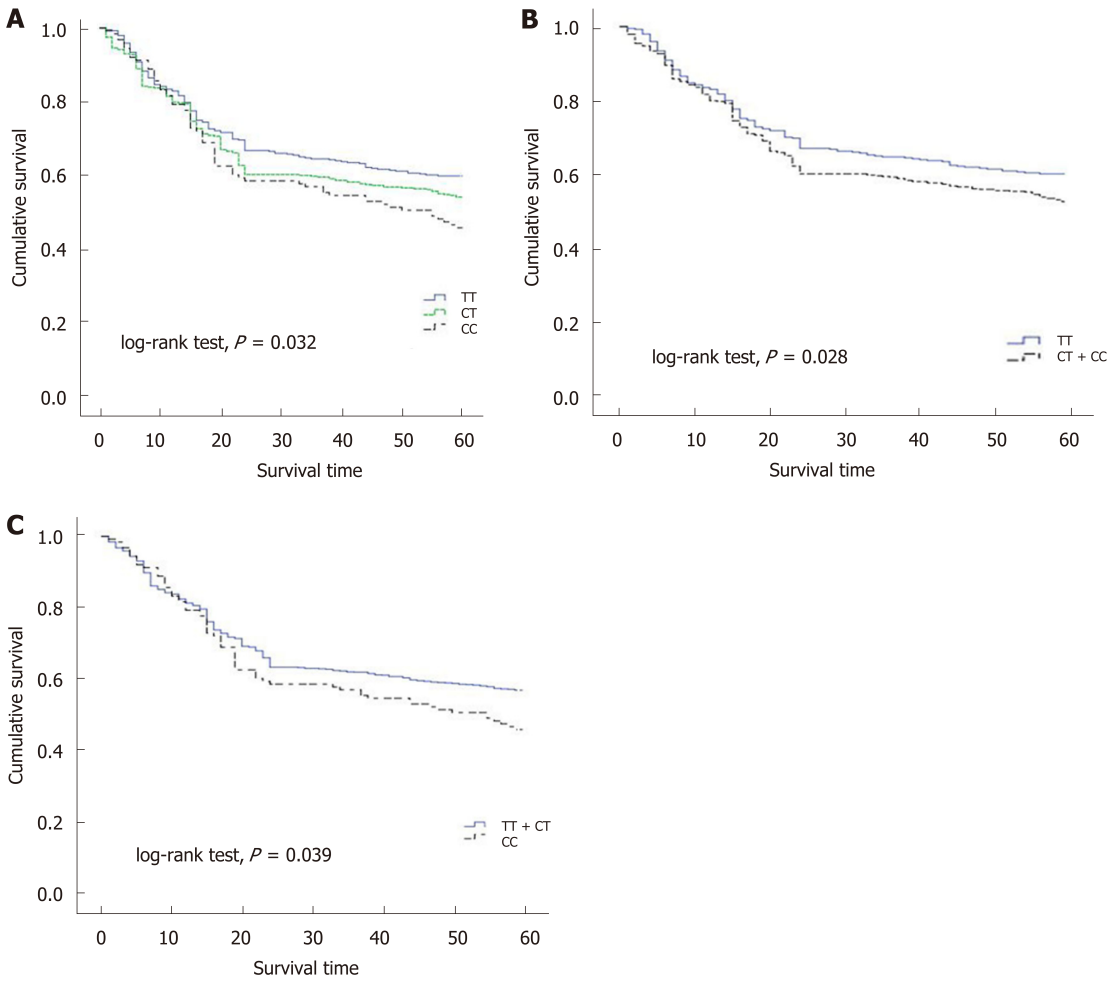

Figure 1 Survival plots of gastric cancer cases stratified by rs2094258 genotype. A: Compared with the survival of cases with no C allele (genotype TT, blue line), cases with one C allele (genotype CT, green line) demonstrated a decreased survival rate and cases with two C alleles (genotype CC, dotted line) exhibited the lowest survival rate; B: Compared with the survival of cases with no C allele (genotype TT, blue line), cases with recessive allele (genotype CT + CC, dotted line) demonstrated a decreased survival rate; C: In the dominant model, case with CC allele showed a lower survival rate compared with cases with dominant allele.

ARTICLE HIGHLIGHTS

Research background

Gastric cancer (GC) is one of the leading causes of cancer-related death worldwide, which causes a high social and economic burden. Xeroderma pigmentosum group G (XPG) or ERCC5 may play a key role in DNA repair, thus affecting cancer prognosis. Studies have shown that *XPG* SNPs may affect the development of cancer such as lung cancer, colorectal cancer, and breast cancer.

Research motivation

Only a few studies have explored the relationships between *XPG* gene SNPs and GC, and the results are inconsistent.

Research objectives

To examine GC risk and survival in relation to common functional *XPG* SNPs through a case-control study, which might improve our understanding of GC and provide new therapeutic targets for this malignancy.

Research methods

A total of 956 histologically confirmed GC cases and 1012 controls were matched by sex, age (within 5 years), and residential district. Cases were followed and the survival time was recorded. DNA was extracted from peripheral blood samples of all cases and controls. *XPG* rs2094258, rs751402, rs2296147, rs1047768, and rs873601 polymorphisms were genotyped using PCR-RFLP. Logistic regression and Cox regression were used for analyzing associations of *XPG* SNPs with risk of GC and prognosis, respectively.

Research results

We found that GC patients with the rs2094258 CT + CC genotype showed a worse survival than those with the TT genotype, and patients with the CC genotype had a tendency of unfavorable prognosis compared with those with the TT + CT genotype. The increase in the number of C alleles of rs2094258 was associated with the long-term survival of GC cases. Other risk factors for survival included tumor differentiation, lymphovascular invasion, and use of chemotherapy. However, the exact mechanisms by which *XPG* SNPs influence GC survival remain to be solved.

Research conclusions

The *XPG* rs2094258 polymorphism may be associated with overall survival in patients with GC.

Research perspectives

If confirmed by other studies, the results of our study suggest that *XPG* rs2094258 polymorphisms may serve as genetic biomarkers for GC prognosis, and may provide clues to biological underpinnings of GC progression.

ACKNOWLEDGEMENTS

We thank all the subjects and researchers who participated in this study.

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