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Original Article

Lack of association between XPC Lys939Gln polymorphism and prostate cancer risk: an updated meta-analysis based on 3039 cases and 3253 controls

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Abstract: Several studies have evaluated the relationship between xeroderma pigmentosum complementation group C (*XPC*) variants and prostate cancer (PCa) risk. However, the results remain inconclusive. The objective of this study was to identify the role of *XPC* Lys939Gln variant on PCa occurrence. Relevant case-control studies published between 2000 and 2014 were retrieved in electronic databases. The pooled odds ratio (ORs) and 95% confidence interval (CI) were employed to calculate the strength of association. Finally, a total of eight articles including 3039 PCa patients and 3203 healthy controls were screened out. Our results found that the frequency of C allele was a little higher in PCa cases than that in control, but it was not associated with the increased risk of PCa (C vs. A: OR=1.05, 95% CI=0.98-1.13, P=0.19). This insignificant association was also observed in other genetic models (P>0.05). In subgroup analysis by ethnicity, no significant relationship was found in any study-population (Asian, Caucasian and African) as well. In conclusions, our results indicated that *XPC* Lys939Gln polymorphism was not associated with PCa susceptibility. Further large well-designed epidemiologic studies with gene-gene and gene-environment interaction should be included and considered.

Keywords: Prostate cancer, *XPC*, polymorphism, meta-analysis

Introduction

Prostate cancer (PCa) is the second most common diagnosed non-skin cancer and the sixth leading cause of cancer death in males [1], accounting for 27% of total male cancers. According to cancer statistics, about 233000 new cases and 29480 death are estimated to have occurred in 2014 among men in the United States [2]. The well-established risk factors: smoking [3], alcohol [4] and family history [5] have been proven to be involved in PCa occurrence. However, the specific mechanisms of PCa progression remain largely unknown. Epidemiologic studies have shown that approximately 42% of all PCa risk factors can be attributed to genetic influences [6], and the genetic-environmental interaction may explain the ethnic difference and geographical variations in the incidence and mortality [7]. Early detection of PCa in asymptomatic average risk men will contribute to the reduced incidence and mortality [8]. Therefore, exploring more new gene indicators for PCa risk is valuable.

During the last decades, genomic rearrangements have drawn public attention. Many studies have shown that genetic variants, resulting from transcriptional or chromatin aberrancies, engage in prostate carcinogenesis mechanisms [9]. Nucleotide excision repair (NER), one major DNA-repair pathway in human cells, involved in DNA damage repair, is the primary defense mechanism against mutagenic exposure [10]. Xeroderma pigmentosum complementation group C (*XPC*), located on human chromosome 3p25, is the primary initiating factor in the global genome NER [11]. *XPC* is a 940-residue DNA binding protein, stimulating repair of oxidative lesions by base excision repair [12]. Mutation of this gene can result in human carcinogenesis. Several most common single nucleotide polymorphisms (SNPs) of *XPC* have been identified. Among which, rs2228001 in exon 15, an A to C substitution at position 939 leading to Lysine to Glutamine replacement, was the most studied site. It has been shown that *XPC* Lys939Gln polymorphism may be a risk factor for bladder carcinogenesis [13], urinary bladder cancer

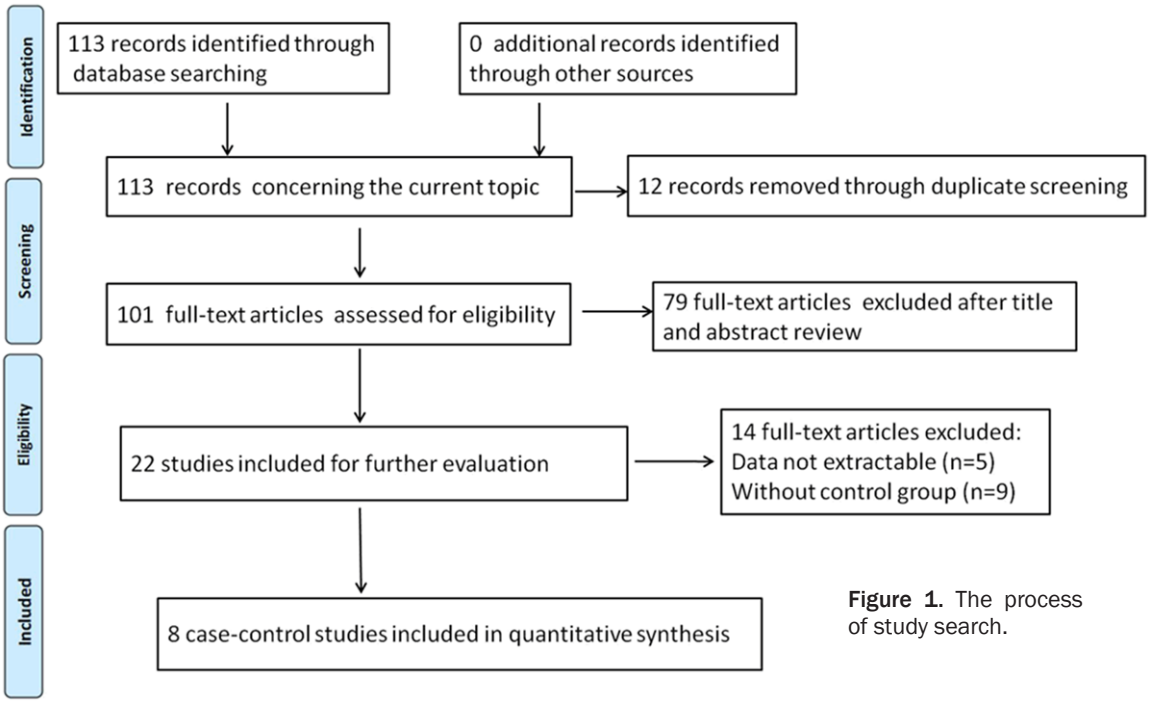

Figure 1. The process of study search.

susceptibility [14], lung cancer risk [15], and colorectal cancer susceptibility [16].

Although a number of case-control studies have investigated the association between *XPC* Lys939Gln polymorphism and PCa risk, the results of these studies were controversial. Hirata et al. suggested that *XPC* Lys939Gln might be risk factors for PCa in Japanese; while, Yang et al. demonstrated that *XPC* Lys939Gln was not associated with the increased risk of PCa [17]. Thus, we conducted this meta-analysis to systematically reevaluate the role of *XPC* Lys939Gln polymorphism in the risk of developing PCa.

Materials and methods

Search strategy

We conducted a systematical literature search on electronic databases of PubMed, Embases and Medline to retrieve the related articles published between January 2000 and December 2014. The following terms: "prostate cancer or prostatic carcinoma", "xeroderma pigmentosum complementation group C or *XPC*" and "polymorphism or variant or mutation" as well as their combinations were employed as the search words. References of retrieved articles were screened manually. When the same authors or laboratories reported the similar issue on the same populations, only the most recent articles were included.

Inclusion and exclusion criteria

The eligible articles had to meet the following criteria: 1) case-control studies; 2) evaluating the relationship between *XPC* Lys939Gln polymorphisms and PCa risk; 3) the patients should be histopathologically confirmed, the controls should be unrelated, cancer free, age- and sex-matched healthy individuals of similar ethnicity; and 4) the results were presented in odd ratios (ORs) with its corresponding 95% confidence interval (CI), and the genotype information was available to extract.

The exclusion criteria were as follows: 1) duplicated reports from the same authors or laboratories; 2) reviews or conference papers; 3) non-English written articles; and 4) without control group or controls were not race-matched.

Date extraction

Two investigators independently assessed the related data provided by authors of each study. Each item should be final reached a consensus. The following details were extracted from each article: first author, publication year, coun-

Table 1. Main characteristics of included studies in this meta-analysis

First author	Year	Country	Ethnicity	Mean age (range)		Sample size		Genotype method
				Cases	Controls	Cases	Controls	
Hirata H	2007	Japan	Asian	68±5	67±15	165	135	PCR-RFLP
Agalliu I-a	2010	USA	Caucasian	70.2 (35-74)	69.3 (35-74)	1308	1266	GeneMapper
Agalliu I-b	2010	USA	African	65.6 (35-74)	64.1 (35-74)	149	85	GeneMapper
Liu Y	2012	China	Asian	70.7±8.4	70.4±10.0	202	221	PCR-RFLP
Mandal RK	2012	India	Caucasian	62.6±8.9	59.1±10.4	192	224	PCR-RFLP
Mittal RD	2012	India	Caucasian	66.0±5.46	64.7±5.71	195	250	PCR-RFLP
Sorour AF	2013	Egypt	African	65.4±8.7	65.4±8.7	50	50	PCR-RFLP
Mirecka A	2014	Poland	Caucasian	68.3 (41-96)	64.6 (35-92)	720	1121	Sequencing
Zhang XJ	2014	China	Asian	66.7±8.2	67.3±7.5	229	264	PCR-MALDI-TOF

PCR-RFLP, polymerase chain reaction-restriction fragment length polymorphism; PCR-MALDI-TOF combined polymerase chain reaction and matrix-assisted laser desorption ionization-time of flight mass spectrometry technologies.

Table 2. Distribution of alleles and genotypes information in *XPC* Lys939Gln polymorphism in included studies

First author	Cases					Controls					
	AA	AC	CC	A	C	AA	AC	CC	A	C	HWE
Hirata H	77	78	10	232	98	72	70	23	214	116	0.67
Agalliu I-a	457	595	205	1509	1005	461	600	190	1522	980	0.97
Agalliu I-b	70	61	16	201	93	36	38	9	110	56	0.98
Liu Y	86	85	31	257	147	102	100	19	304	138	0.73
Mandal RK	93	71	28	257	127	114	94	16	322	126	0.85
Mittal RD	94	73	28	261	129	127	104	19	358	142	0.94
Sorour AF	16	25	9	57	43	18	27	5	63	37	0.53
Mirecka A	214	290	98	718	486	265	384	122	914	628	0.68
Zhang XJ	158	38	33	354	104	170	37	31	377	99	0.00

HWE, hardy-weinberg equilibrium. h.68item should be finalcles; raries.

try, ethnicity, mean age, total number of patients and controls, genotype methods, genotype information, and Hardy-Weinberg equilibrium (HWE) of genotypes in controls.

Statistical analysis

The strength of association was estimated by pooled ORs with its 95% CI according to the methods of Woof. The allelic model (C vs. A), homozygous model (CC vs. AA), heterozygous model (CC vs. AC), dominant model (CC+AC vs. AA) and recessive model (CC vs. AC+AA) were calculated in this study to evaluate the risk. Between-study heterogeneity was evaluated by the Q-test and the I^2 test. The fixed-effects model was used when the *P*-value of Q-test more than 0.1 and I^2 of the I^2 test less than 50% which both indicated homogenous, otherwise, the random-effects model was selected when it was heterogenous. Both funnel plot and Egger's test were used to assess the publication bias (P< 0.10 was considered statistical significance). All statistical analyses were performed using Review Manage (v.5; Oxford, England), and the algorithms was as previous descripted by Deeks et al. [18].

Results

Characteristics of included studies

A total of eight case-control studies were eligible after filtering with the inclusion and exclusion criteria, including 3039 PCa patients and 3203 healthy controls. **Figure 1** showed the searching process. Of the eight articles, one contained two study populations [19]. For ethnicities, three were Asian population [20-22], four were Caucasian population [19, 23-25], and two were African population [19, 26]. The total number of sample size of each study ranged from 100 to 2574. Genotypes of controls in all included studies were accord with HWE except the study conducted by Zhang et al. **Table 1** showed the main characteristics of the included studies. **Table 2** listed the alleles and genotypes information of each study in this meta-analysis.

Meta-analysis

Table 3 presented the results of the relationship between *XPC* Lys939Gln polymorphism and PCa risk. Between-studies heterogeneity

Table 3. Results of total and subgroup meta-analyses

rs2228001	Comparisons	N	OR (95% CI)	P	I^2	PH	Model
Total	C vs. A	9	1.05 (0.98, 1.13)	0.19	16%	0.30	F
	CC vs. AA	9	1.22 (0.93, 1.60)	0.15	53%	0.03	R
	CC vs. AC	9	1.25 (0.94, 1.65)	0.12	55%	0.02	R
	CC+AC vs. AA	9	1.02 (0.92, 1.13)	0.70	0%	0.97	F
	CC vs. AC+AA	9	1.24 (0.95, 1.62)	0.11	58%	0.02	R
Asian	C vs. A	3	1.04 (0.79, 1.37)	0.78	59%	0.07	R
	CC vs. AA	3	1.00 (0.45, 2.22)	0.99	77%	0.01	R
	CC vs. AC	3	0.95 (0.40, 2.25)	0.90	78%	0.01	R
	CC+AC vs. AA	3	1.06 (0.84, 1.34)	0.62	0%	0.62	F
	CC vs. AC+AA	3	0.99 (0.44, 2.21)	0.97	80%	0.007	R
Caucasian	C vs. A	4	1.05 (0.97, 1.14)	0.23	16%	0.31	F
	CC vs. AA	4	1.29 (0.94, 1.77)	0.11	58%	0.07	R
	CC vs. AC	4	1.34 (0.97, 1.85)	0.07	61%	0.05	R
	CC+AC vs. AA	4	1.02 (0.90, 1.14)	0.79	0%	0.86	F
	CC vs. AC+AA	4	1.32 (0.97, 1.81)	0.08	63%	0.05	R
African	C vs. A	2	1.02 (0.74, 1.42)	0.90	0%	0.33	F
	CC vs. AA	2	1.20 (0.57, 2.52)	0.63	0%	0.32	F
	CC vs. AC	2	1.36 (0.66, 2.82)	0.41	0%	0.47	F
	CC+AC vs. AA	2	0.94 (0.60, 1.47)	0.77	0%	0.49	F
	CC vs. AC+AA	2	1.28 (0.64, 2.57)	0.48	0%	0.36	F

N, number of included studies; OR, odds ratio; CI, confidence interval; I^2, the portion of between-study heterogeneity; PH, *p*-value of heterogeneity; F, fixed-effect model; R, random-effect model.

was assessed, and the fixed-effect model was used in the allele model and the dominant model; the random-effect model was used in the homozygous model, the heterozygous model and the recessive model. Overall, we found that the frequency of C allele of *XPC* Lys939Gln polymorphism was a little higher in PCa patients than that in healthy controls (36.7% versus 35.6%). However, the C allele was not associated with increased the risk of PCa (C vs. A: OR=1.05, 95% CI=0.98-1.13, P=0.19) as shown in **Figure 2**. This insignificant association between *XPC* Lys939Gln polymorphism and PCa susceptibility was also observed under any other genetic models (CC vs. AA: OR=1.22, 95% CI=0.93-1.60, P=0.15 (**Figure 3A**); CC vs. AC: OR=1.25, 95% CI=0.94-1.65, P=0.12 (**Figure 3B**); CC+AC vs. AA: OR=1.02, 95% CI=0.92-1.13, P=0.70 (**Figure 3C**); CC vs. AC+AA: OR=1.24, 95% CI=0.95-1.62, P=0.11 (**Figure 3D**).

Subgroup analysis by ethnicity found no significant association among Asians (C vs. A: OR=1.04, 95% CI=0.79-1.37, P=0.78; CC vs. AA: OR=1.00, 95% CI=0.45-2.22, P=0.99; CC vs. AC: OR=0.95, 95% CI=0.40-2.25, P=0.90; CC+AC vs. AA: OR=1.06, 95% CI=0.84-1.34, P=0.62; CC vs. AC+AA: OR=0.99, 95% CI=0.44-2.21, P=0.97), Caucasians (C vs. A: OR=1.05, 95% CI=0.97-1.14, P=0.23; CC vs. AA: OR=1.29, 95% CI=0.94-1.77, P=0.11; CC vs. AC: OR=1.34, 95% CI=0.97-1.85, P=0.07; CC+AC vs. AA: OR=1.02, 95% CI=0.90-1.14, P=0.79; CC vs. AC+AA: OR=1.32, 95% CI=0.97-1.81, P=0.08) and Africans (C vs. A: OR=1.02, 95% CI=0.74-1.42, P=0.90; CC vs. AA: OR=1.20, 95% CI=0.57-2.52, P=0.63; CC vs. AC: OR=1.36, 95% CI=0.66-2.82, P=0.41; CC+AC vs. AA: OR=0.94, 95% CI=0.60-1.47, P=0.77; CC vs. AC+AA: OR=1.2, 95% CI=0.64-2.57, P=0.48) in any genetic models as well.

Publication bias

The symmetry of funnel plot indicated that there was no obvious publication bias in this meta-analysis as shown in **Figure 4**. Egger's test was employed to further assess publication bias, and the results showed the absence of the publication bias (P>0.01).

Discussion

In this meta-analysis, we evaluated the role of *XPC* Lys939Gln polymorphism in PCa susceptibility. Overall, our results showed that *XPC* Lys939Gln polymorphism was not associated with PCa susceptibility. In the subgroup analysis by ethnicity, no significant association was found in three races (Asian, Caucasian and African) as well. Our results were consistent with previous meta-analysis (five separate case-control studies including 1966 cases and 1970 controls) which showed that this variant not likely contributed to susceptibility to PCa [27].

PCa is the most frequent cancer among males in economically developed countries. The pathogenesis of PCa is likely involved the genetic

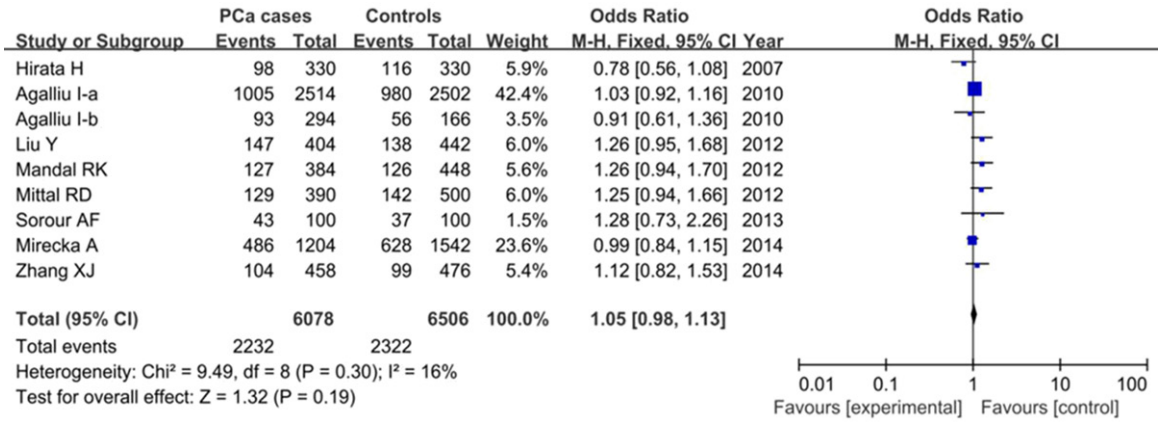

Figure 2. Forest plots of *XPC* Lys939Gln polymorphism and prostate cancer susceptibility under the allele model.

factors. Genetic variants may contribute to PCa risk. Numerous genetic variants in the DNA repair pathway have been explored. *XPC* protein, a DNA damage recognition factor, involves in initiating GG-NER pathway by recognizing the DNA lesion and recruiting downstream factors. It not only functions as an early damage sensor in open complex formation and in repair of complex protein formations, but also in the removal of oxidative DNA damage and redox homeostasis and cell-cycle control [28]. *XPC* expression is regulated by p53 at the transcriptional level. It has been identified a functional p53 response element in vivo in the coding sequence of the *XPC* protein [29]. In cells, *XPC* forms a complex with the HR23B [30] and Centrin2 proteins [31]. *XPC*-HR23B has previously been shown to be necessary and sufficient to support NER activity in vitro [32]. Moreover, *XPC* expression could be enhanced by SIRT1 through reducing AKT-dependent nuclear localization of *XPC*-transcription repressor [33].

XPC expression may be involved in the process of cancer development and associated with cancer risk. Hsiao et al. found that the expression of nuclear *XPC* was significantly lower in cutaneous squamous cell carcinoma compared with their adjacent normal epidermis, and proved that the decreased *XPC* expression was associated with recurrent rate and high-risk cutaneous squamous cell carcinoma [34]. Lai et al. observed that *XPC* protein expression correlated with tumor stage, cigarette smoking and poor survival; and *XPC* expression could predict drug resistance in patients with lung adenocarcinoma [35]. Bai et al. firstly investigated *XPC* expression in sporadic breast cancer tissues, and showed that *XPC* was involved in the initiation and progression of breast cancer [36]. In addition, genetic variants may influence the *XPC* expression, leading to the progression of disease. Qiao et al. identified two 3'UTR variants of *XPC* which might be associated with bladder cancer risk [37]. Berger et al. demonstrated that *XPC* coding variants could affect protein function, and/or 3'UTR variants result in an altered protein levels via allele-specific mIR binding [38]. Cartault et al. found that a new G to C homozygous substitution at 3'-end of *XPC* in intron 12 (IVS 12-1G/C) in the patients leads to the abolition of an acceptor splicing site and the absence of the *XPC* protein; and the highest worldwide prevalence of xeroderma pigmentosum are in black Mahori patients [39]. These findings indicate that *XPC* may play a role in prevention of human carcinogenesis.

Several mutations have been identified in *XPC* gene. *XPC* Lys939Gln A/C polymorphism has been shown to play an important role in digestive system cancer susceptibility [40] and significantly increase the risk of lung cancer in Asian population [41]; and it is also deemed to be involved in modulating colorectal cancer susceptibility independently or jointly [42]. *XPC* PAT+/- polymorphism has been proven to associate with urinary system cancer risk [43], and contribute to the risk for developing bladder cancer in a Chinese Han population [44]. *XPC* Ala499Val is shown to significantly associate with lung and breast cancer risk [45], and bladder cancer susceptibility [46]. However, no association was found between polymorphisms of *XPC* Lys939Gln or Ala499Val and helicobacter pylori infection-related gastric antrum

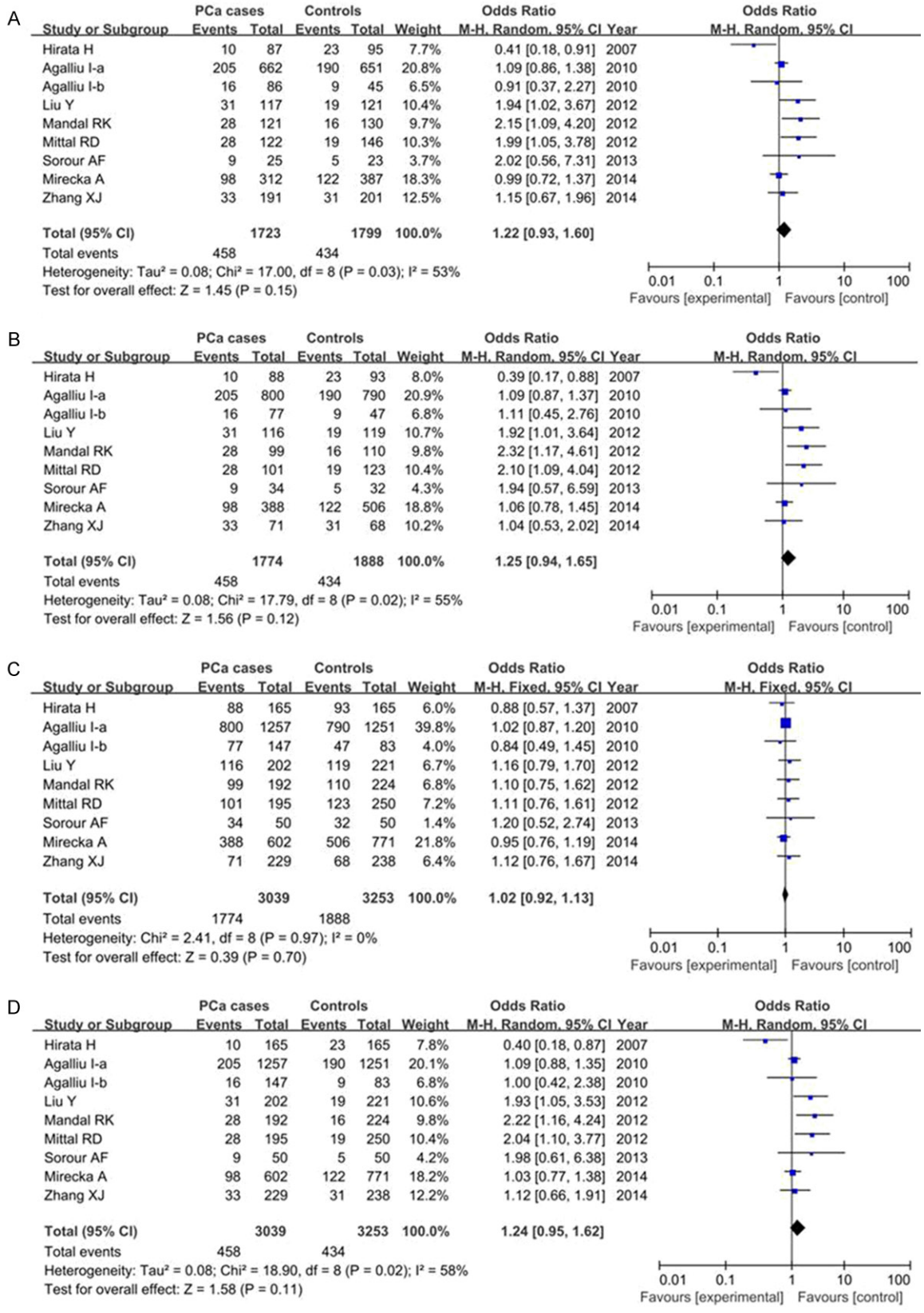

Figure 3. Meta-analysis of the association between *XPC* Lys939Gln polymorphism and prostate cancer risk under genotype models: A. The homozygous model (CC vs. AA); B. The heterozygous model (CC vs. AC); C. The dominant model (CC+AC vs. AA); D. The recessive model (CC vs. AC+AA).

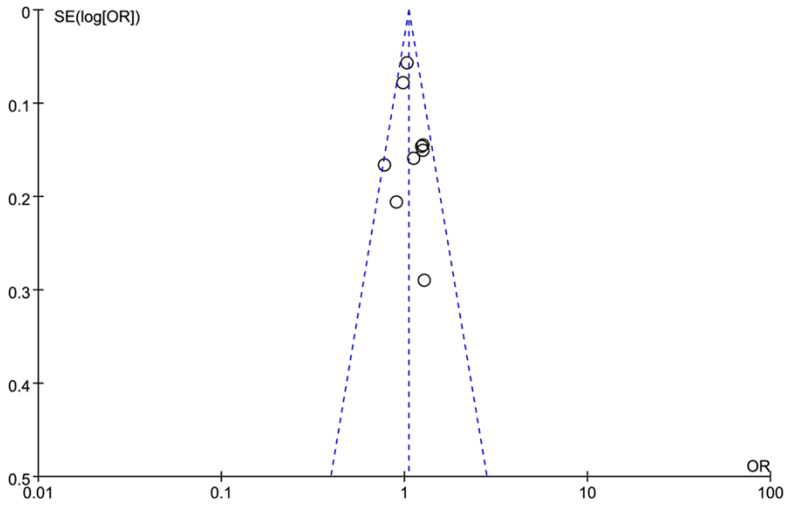

Figure 4. Funnel plot on the association for allelic model (C vs. A) of Lys939Gln polymorphism on *XPC* gene and PCa risk in a fixed-effects model.

adenocarcinoma susceptibility in Chinese population [47]. A meta-analysis conducted by Peng et al. found that the *XPC* polymorphisms (Lys939Gln, Val499Arg, and PAT-/+) did not associate with gastric cancer risk [48]. *XPC* PAT-/+ polymorphism allele might be a low-penetrant risk factor for developing breast cancer [49], and not associated with increasing cutaneous melanoma risk [50] and colorectal cancer [51].

Several limitations were presented in previous meta-analysis. Firstly, the clinical stages of patients with PCa could not be extracted from the included studies. In the future researches, we should consider the genetic polymorphisms in each stage of PCa. Secondly, significant heterogeneity between studies was presented, which may influence the results. Thirdly, the number of included studies was small. Fourthly, the mean ages of patients were a little older, while other age groups should also be included. Lastly, other *XPC* variants or risk factors should be taken into account, moreover, gene-gene and gene-environment interactions should be considered.

In conclusion, our results found no significant association between *XPC* Lys939Gln polymorphism and PCa development. Future well-designed studies involving different ethnic populations are still needed to further investigate the role of *XPC* Lys939Gln polymorphism in PCa risk.

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Disclosure of conflict of interest

None.

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References

[1] Jemal A, Bray F, Center MM, Ferlay J, Ward E and Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61: 69-90.

[2] Siegel R, Ma J, Zou Z and Jemal A. Cancer statistics, 2014. CA Cancer J Clin 2014; 64: 9-29.

[3] Murphy AB, Akereyeni F, Nyame YA, Guy MC, Martin IK, Hollowell CM, Walker K, Kittles RA and Ahaghotu C. Smoking and prostate cancer in a multi-ethnic cohort. Prostate 2013; 73: 1518-1528.

[4] McGregor SE, Courneya KS, Kopciuk KA, Tosevski C and Friedenreich CM. Case-control study of lifetime alcohol intake and prostate cancer risk. Cancer Causes Control 2013; 24: 451-461.

[5] Taherian N, Hamel N, Begin LR, Bismar TA, Goldgar DE, Feng BJ and Foulkes WD. Familial prostate cancer: the damage done and lessons learnt. Nat Rev Urol 2013; 10: 116-122.

[6] Hsing AW and Chokkalingam AP. Prostate cancer epidemiology. Front Biosci 2006; 11: 1388-1413.

[7] Plata Bello A and Concepcion Masip T. Prostate cancer epidemiology. Arch Esp Urol 2014; 67: 373-382.

[8] Carter HB, Albertsen PC, Barry MJ, Etzioni R, Freedland SJ, Greene KL, Holmberg L, Kantoff P, Konety BR, Murad MH, Penson DF and Zietman AL. Early detection of prostate cancer: AUA Guideline. J Urol 2013; 190: 419-426.

[9] Berger MF, Lawrence MS, Demichelis F, Drier Y, Cibulskis K, Sivachenko AY, Sboner A, Esgueva R, Pflueger D, Sougnez C, Onofrio R, Carter SL, Park K, Habegger L, Ambrogio L, Fennell T, Parkin M, Saksena G, Voet D, Ramos AH, Pugh TJ,

Wilkinson J, Fisher S, Winckler W, Mahan S, Ardlie K, Baldwin J, Simons JW, Kitabayashi N, MacDonald TY, Kantoff PW, Chin L, Gabriel SB, Gerstein MB, Golub TR, Meyerson M, Tewari A, Lander ES, Getz G, Rubin MA and Garraway LA. The genomic complexity of primary human prostate cancer. Nature 2011; 470: 214-220.

[10] Chen ZP, Malapetsa A, Monks A, Myers TG, Mohr G, Sausville EA, Scudiero DA and Panasci LC. Nucleotide excision repair protein levels vis-a-vis anticancer drug resistance in 60 human tumor cell lines. Ai Zheng 2002; 21: 233-239.

[11] Hoogstraten D, Bergink S, Ng JM, Verbiest VH, Luijsterburg MS, Geverts B, Raams A, Dinant C, Hoeijmakers JH, Vermeulen W and Houtsmuller AB. Versatile DNA damage detection by the global genome nucleotide excision repair protein XPC. J Cell Sci 2008; 121: 2850-2859.

[12] Shell SM, Hawkins EK, Tsai MS, Hlaing AS, Rizzo CJ and Chazin WJ. Xeroderma pigmentosum complementation group C protein (XPC) serves as a general sensor of damaged DNA. DNA Repair (Amst) 2013; 12: 947-953.

[13] Zhang Y, Wang X, Zhang W and Gong S. An association between XPC Lys939Gln polymorphism and the risk of bladder cancer: a meta-analysis. Tumour Biol 2013; 34: 973-982.

[14] Dou K, Xu Q and Han X. The association between XPC Lys939Gln gene polymorphism and urinary bladder cancer susceptibility: a systematic review and meta-analysis. Diagn Pathol 2013; 8: 112.

[15] Zhu ML, Hua RX and Zheng L. Associations between polymorphisms of the XPC gene and lung cancer susceptibility: a meta-analysis. Tumour Biol 2014; 35: 2931-2939.

[16] Peng Q, Lao X, Tang W, Chen Z, Li R, Qin X and Li S. XPC Lys939Gln polymorphism contributes to colorectal cancer susceptibility: evidence from a meta-analysis. Diagn Pathol 2014; 9: 120.

[17] Yang B, Chen WH, Wen XF, Liu H and Liu F. Role of DNA repair-related gene polymorphisms in susceptibility to risk of prostate cancer. Asian Pac J Cancer Prev 2013; 14: 5839-5842.

[18] Deeks JJ and Higgins JP. Statistical algorithms in Review Manager 5. Statistical Methods Group of The Cochrane Collaboration 2010; 1-11.

[19] Agalliu I, Kwon EM, Salinas CA, Koopmeiners JS, Ostrander EA and Stanford JL. Genetic variation in DNA repair genes and prostate cancer risk: results from a population-based study. Cancer Causes Control 2010; 21: 289-300.

[20] Hirata H, Hinoda Y, Tanaka Y, Okayama N, Suehiro Y, Kawamoto K, Kikuno N, Majid S, Vejdani K and Dahiya R. Polymorphisms of DNA repair genes are risk factors for prostate cancer. Eur J Cancer 2007; 43: 231-237.

[21] Liu Y, Chen Z, Wei Q, Yuan F, Zhi Y, Song B and Yang J. Poly (AT) polymorphism in the XPC gene and smoking enhance the risk of prostate cancer in a low-risk Chinese population. Cancer Genet 2012; 205: 205-211.

[22] Zhang XJ, Liu P and Zhu F. Polymorphisms of DNA repair-related genes with susceptibility and prognosis of prostate cancer. Genet Mol Res 2014; 13: 4419-4424.

[23] Mirecka A, Paszkowska-Szczur K, Scott RJ, Gorski B, van de Wetering T, Wokolorczyk D, Gromowski T, Serrano-Fernandez P, Cybulski C, Kashyap A, Gupta S, Golab A, Slojewski M, Sikorski A, Lubinski J and Debniak T. Common variants of xeroderma pigmentosum genes and prostate cancer risk. Gene 2014; 546: 156-161.

[24] Mandal RK, Gangwar R, Kapoor R and Mittal RD. Polymorphisms in base-excision & nucleotide-excision repair genes & prostate cancer risk in north Indian population. Indian J Med Res 2012; 135: 64-71.

[25] Mittal RD, Mandal RK and Gangwar R. Base excision repair pathway genes polymorphism in prostate and bladder cancer risk in North Indian population. Mech Ageing Dev 2012; 133: 127-132.

[26] Sorour AF, Talaat IM, Youssif TMA and Atta MA. Detection of Polymorphisms of DNA Repair Genes (XRCC1 and XPC) in Prostate Cancer. Journal of Cancer Therapy 2013; 4: 1499.

[27] Zou YF, Tao JH, Ye QL, Pan HF, Pan FM, Su H and Ye DQ. Association of XPC gene polymorphisms with susceptibility to prostate cancer: evidence from 3,936 subjects. Genet Test Mol Biomarkers 2013; 17: 926-931.

[28] Wang G, Wang L, Bhoopalan V, Xi Y, Bhalla DK, Wang D and Xu XS. The role of XPC protein deficiency in tobacco smoke-induced DNA hypermethylation of tumor suppressor genes. Open Journal of Genetics 2013; 3: 285.

[29] Hastak K, Adimoolam S, Trinklein ND, Myers RM and Ford JM. Identification of a Functional In Vivo p53 Response Element in the Coding Sequence of the Xeroderma Pigmentosum Group C Gene. Genes Cancer 2012; 3: 131-140.

[30] Sugasawa K, Masutani C, Uchida A, Maekawa T, van der Spek PJ, Bootsma D, Hoeijmakers JH and Hanaoka F. HHR23B, a human Rad23 homolog, stimulates XPC protein in nucleotide excision repair in vitro. Mol Cell Biol 1996; 16: 4852-4861.

[31] Nishi R, Okuda Y, Watanabe E, Mori T, Iwai S, Masutani C, Sugasawa K and Hanaoka F. Centrin 2 stimulates nucleotide excision repair by interacting with xeroderma pigmentosum

group C protein. Mol Cell Biol 2005; 25: 5664-5674.
[32] Araujo SJ, Tirode F, Coin F, Pospiech H, Syvaoja JE, Stucki M, Hubscher U, Egly JM and Wood RD. Nucleotide excision repair of DNA with recombinant human proteins: definition of the minimal set of factors, active forms of TFIIH, and modulation by CAK. Genes Dev 2000; 14: 349-359.
[33] Ming M, Shea CR, Guo X, Li X, Soltani K, Han W and He YY. Regulation of global genome nucleotide excision repair by SIRT1 through xeroderma pigmentosum C. Proc Natl Acad Sci U S A 2010; 107: 22623-8.
[34] Hsiao YP, Chao WR and Wey SJ. Decreased Expression of Xeroderma Pigmentosum Group C (XPC) Protein in Cutaneous Squamous Cell Carcinoma. Life Science Journal 2014; 11.
[35] Lai TC, Chow KC, Fang HY, Cho HC, Chen CY, Lin TY, Chiang IP and Ho SP. Expression of xeroderma pigmentosum complementation group C protein predicts cisplatin resistance in lung adenocarcinoma patients. Oncol Rep 2011; 25: 1243-1251.
[36] Bai X, Jin F, Fu Y, Yu Z, Zhao L, Ren J, Li Y, Jiao X, Zhao H, Yao W, Mi X, Wang E, Olopade OI, Zhou M and Wei M. Clinicopathological significance and prognostic value of Xeroderma pigmentosum complementary group C (XPC) expression in sporadic breast cancer patients. Med Oncol 2012; 29: 1543-1553.
[37] Qiao B, Scott GB, Elliott F, Vaslin L, Bentley J, Hall J, Bishop DT, Knowles MA and Kiltie AE. Functional assays to determine the significance of two common XPC 3'UTR variants found in bladder cancer patients. BMC Med Genet 2011; 12: 84.
[38] Berger F, Vaslin L, Belin L, Asselain B, Forlani S, Humbert S, Durr A and Hall J. The impact of single-nucleotide polymorphisms (SNPs) in OGG1 and XPC on the age at onset of Huntington disease. Mutat Res 2013; 755: 115-119.
[39] Cartault F, Nava C, Malbrunot AC, Munier P, Hebert JC, N'Guyen P, Djeridi N, Pariaud P, Pariaud J, Dupuy A, Austerlitz F and Sarasin A. A new XPC gene splicing mutation has lead to the highest worldwide prevalence of xeroderma pigmentosum in black Mahori patients. DNA Repair (Amst) 2011; 10: 577-585.
[40] Jiang X, Zhou LT, Zhang SC and Chen K. XPC Polymorphism Increases Risk of Digestive System Cancers: Current Evidence from A Meta-Analysis. Chin J Cancer Res 2012; 24: 181-189.
[41] Jin B, Dong Y, Zhang X, Wang H and Han B. Association of XPC polymorphisms and lung cancer risk: a meta-analysis. PLoS One 2014; 9: e93937.
[42] Wu Y, Jin M, Liu B, Liang X, Yu Y, Li Q, Ma X, Yao K and Chen K. The association of XPC polymorphisms and tea drinking with colorectal cancer risk in a Chinese population. Mol Carcinog 2011; 50: 189-198.
[43] Dai QS, Hua RX, Zhang R, Huang YS, Hua ZM, Yun CT, Zeng RF and Long JT. Poly (AT) deletion/insertion polymorphism of the XPC gene contributes to urinary system cancer susceptibility: a meta-analysis. Gene 2013; 528: 335-342.
[44] Liu Y, Wang H, Lin T, Wei Q, Zhi Y, Yuan F, Song B, Yang J and Chen Z. Interactions between cigarette smoking and XPC-PAT genetic polymorphism enhance bladder cancer risk. Oncol Rep 2012; 28: 337-345.
[45] He J, Shi TY, Zhu ML, Wang MY, Li QX and Wei QY. Associations of Lys939Gln and Ala499Val polymorphisms of the XPC gene with cancer susceptibility: a meta-analysis. Int J Cancer 2013; 133: 1765-1775.
[46] Wang Y, Li Z, Liu N and Zhang G. Association between CCND1 and XPC polymorphisms and bladder cancer risk: a meta-analysis based on 15 case-control studies. Tumour Biol 2014; 35: 3155-3165.
[47] Long XD, Ma Y, Huang YZ, Yi Y, Liang QX, Ma AM, Zeng LP and Fu GH. Genetic polymorphisms in DNA repair genes XPC, XPD, and XRCC4, and susceptibility to Helicobacter pylori infection-related gastric antrum adenocarcinoma in Guangxi population, China. Mol Carcinog 2010; 49: 611-618.
[48] Peng Q, Chen Z, Lu Y, Lao X, Mo C, Li R, Qin X and Li S. Current evidences on XPC polymorphisms and gastric cancer susceptibility: a meta-analysis. Diagn Pathol 2014; 9: 96.
[49] Zheng W, Cong XF, Cai WH, Yang S, Mao C and Zou HW. Current evidences on XPC polymorphisms and breast cancer susceptibility: a meta-analysis. Breast Cancer Res Treat 2011; 128: 811-815.
[50] Zhou L, Lu Y, Yang G and Wu J. Quantitative assessment of the association between XPC Lys939Gln polymorphism and cutaneous melanoma risk. Tumour Biol 2014; 35: 1427-1432.
[51] Liu C, Yin Q, Ying M, Lin J, Li L, Jiao G, Wang M and Wang Y. XPC Lys939Gln and Ala499Val polymorphisms in colorectal cancer susceptibility: a meta-analysis of case-control studies. Mol Biol Rep 2014; 41: 1171-1178.