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XPC exon15 Lys939Gln variant increase susceptibility to prostate adenocarcinoma

Evidence based on 4306 patients and 4779 controls

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Abstract

Background: Previous studies have investigated the correlation between xeroderma pigmentosumcomplementation group C (XPC) variants and prostate adenocarcinoma (PA) risk. Nevertheless, research findings remain inconclusive.

Methods: We conducted a pooled analysis to obtain a more accurate estimation of the relationship on XPC exon15 Lys939Gln polymorphism with susceptibility to PA. Moreover, in silico tools were employed to investigate the effect of XPC expression on PA patients' survival time.

Results: A total of 4306 patients and 4779 control subjects were assessed. The overall results indicated that XPC Lys939Gln variant was associated with PA risk (recessive genetic model: odds ratio = 1.15, 95% confidence interval = 1.02–1.30, $P_{heterogeneity}$ = .044, P = .021, I^2 = 45.2), especially in Asian descendants. Population-based studies revealed similar results (odds ratio = 1.15, 95% confidence interval = 1.01–1.32, $P_{heterogeneity}$ = .146, P = .040, I^2 = 39.0). In silico tools showed that XPC expression in Caucasian patients was lower than in the normal group. No positive association was observed in African patients. PA subjects with high XPC expression had a longer overall survival time than low expression group.

Conclusion: Our findings indicated that XPC Lys939Gln variant might contribute to increased PA susceptibility, especially for Asian patients.

Abbreviations: HB = hospital based, HWE = Hardy–Weinberg equilibrium of controls, NA = not available, PA = prostate adenocarcinoma, PB = population based, XPC = xeroderma pigmentosumcomplementation group C, ZFYVE20 = Rabenosyn-5.

Keywords: analysis, prostate adenocarcinoma, variant, xeroderma pigmentosumcomplementation group C

1. Introduction

Prostate adenocarcinoma (PA) remains the most common malignancies among male worldwide. Previous studies showed that PA was the third and second major cause of male mortality in Europe and America.[1,2] National Cancer Institute estimated that approximately 164,690 new PA cases was diagnosed in 2018, with more than 3 million men suffering from this disease in the United States (https://seer.cancer.gov/csr/1975_2015). Although there are epidemiologic differences between the PA incidence and mortality rates in Western and Asian countries, the incidence rate of this cancer type in Asia has increased tremendously in recent years.[3,4] Until now, the detailed mechanisms and exact etiology of PA remains unclear.[5] In addition, the prevention and treatment for PA is still complicated depending on the stage of disease and the choice of single patient.[6] Therefore, it is urgent to update the molecular mechanism of PA pathogenesis and explore new targeted therapies.

It has been shown that genetic factors could play pivotal roles in the development of PA. For instance, a decline in DNA repair was reported as a key factor in the progression of PA.[7] Nucleotide excision repair (NER), the major defense mechanism of antimutagenic exposure, is known as the main DNA repair pathway in human.[8] Xeroderma pigmentosum complementation group C (XPC), an integral part of the NER pathway, can bind reticulum-associated degradation B (Rad) 23 and participate in early damage identification and initiation of NER.[9] XPC gene is located on human c3p25.[10] Mutation of this gene could alter NER capacity and result in human carcinogenesis.[11] One of the most extensively studied polymorphism of XPC is an A to C substitution at position 939, resulting in the replacement of lysine to glutamine (Lys939Gln, rs2228001).[12]

Previous studies have shown that XPC Lys939Gln variant is a risk factor for bladder cancer,[13] colorectal cancer,[14] and lung

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FQ, SLG, KX, QXS, and ZZ contributed equally to the work.

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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cancer.[15] Association between this polymorphism and PA risk has also been previously studied.[16–20] However, the relationship between XPC Lys939Gln polymorphism and PA susceptibility in different case–control studies is not clear. Therefore, a comprehensive analysis based on all eligible data according to the inclusion criteria was performed to further explore the correlation between XPC Lys939Gln variant and PA risk.[16–26]

2. Methods

2.1. Search strategy

A comprehensive literature search was conducted on electronic databases, such as Web of Science, Google Scholar, PubMed, and China Wanfang Databases to retrieve all publications on XPC exon15 Lys939Gln polymorphism and PA susceptibility. The following terms were employed: "XPC OR xeroderma pigmentosumcomplementation group C," "polymorphism OR mutation OR variant," and "carcinoma OR adenocarcinoma OR cancer." Last search was performed on November 28, 2019. Furthermore, references of eligible publications were also screened to maximize the coverage of searches. If there were overlapping data based on the same population, we only selected the latest or the largest study.

2.2. Study selection and inclusion criteria

Two investigators independently screened the articles for compliance with inclusion criteria. Eligible studies in the current analysis should meet all the following criteria: investigated the relationship between XPC exon15 Lys939Gln polymorphism and PA risk; contained available genotype frequency for calculating odds ratio; and utilized a case–control design.

2.3. Exclusion criteria

The exclusion criteria were: studies without control data; articles did not contain available genotype frequency for pooled analysis; conference papers or reviews; and overlapping data from the same laboratories or authors.

2.4. Data extraction

All relevant data were independently assessed by two of the authors. The following information was extracted from each study: first authors' name, publication year, ethnicity of participants, source of control, sample size of case and control group, genotyping data of XPC exon15 Lys939Gln polymorphism in cases and controls, age range, P value of Hardy–Weinberg equilibrium (HWE) in control, genotyping method. If the disagreement existed, it should be resolved by discussion with a 3rd investigator.

2.5. Methods for quantitative synthesis

The overall association between XPC exon15 Lys939Gln polymorphism and PA risk was calculated through odds ratio and 95% confidence interval (CI). Four genetic models were applied in the present analysis: allelic comparison (Gln-allele vs Lys-allele, or C-allele vs A-allele), homozygote contrast (Gln/Gln vs Lys/Lys), dominant genetic model (Gln/Gln + Gln/Lys vs Lys/Lys), and recessive model (Gln/Gln vs Gln/Lys + Lys/Lys). I^2 test and Q test was adopted to assess P value of heterogeneity. If $I^2 <$ 50% or P value of Q test more than .005, the fixed-effects model (Mantel–Haenszel method) is employed. Otherwise, the random-effects model (DerSimonian–Laird method) would be conducted.[27,28] The qualitative funnel plot was performed to investigate publication bias by measuring standard error of log (odds ratio [OR]) for single research plotted against its OR. HWE was measured by chi-square test. P value $>.05$ indicated an HWE balance. Stratified analysis contained types of ethnicity and source of control. The present analyses were carried out using STATA software v11.0 (Stata Corporation, Lakeway, TX).

2.6. Expression of XPC utilizing in silico analysis

We employed the online gene expression database to further evaluate the expression of XPC in PA tissues as well as the paracancerous tissues (http://gemini.cancer-pku.cn/).[29] A total of 549 participants were included in this database for investigating the XPC expression in prostate tissues. The Cancer Genome Atlas (TCGA) samples were also applied to demonstrate the effect of high and low expression of XPC on PA risk and overall survival (OS) probability (http://genomics.jefferson.edu/proggene/intro.php). Furthermore, we adopt the online database (http://gepia.cancer-pku.cn/index.html) to explore the gene–gene correlation regarding XPC.

3. Results

3.1. Studies characteristics

As shown in Table 1, a total of 11 publications describing 12 case–control studies on XPC exon15 Lys939Gln polymorphism were eventually retrieved in the current analysis. The study conducted by Yang et al[30] contained overlapping data compared to that by Zhang et al.[23] Therefore, we only choose the latest study by Zhang et al. A totally of 4306 PA patients and 4779 control subjects were enrolled in the current analysis. Moreover, we investigated minor allele frequencies of XPC Lys939Gln (rs2228001A/C) polymorphism reported in the main worldwide populations: in Africans, 0.249; Europeans, 0.405; Americans, 0.280; East Asians, 0.333; South Asians, 0.320; and Global, 0.315 (Fig. 1). In subgroup analysis by race, a total of 7 studies were based on Asian populations, 2 studies focused on Caucasian populations, 2 analyzed African populations, and the rest focused on Arabians. In stratified analysis by source of control, there were 6 hospital-based studies and the rest 6 studies were performed utilizing population-based controls. polymerase chain reaction-restriction fragment length polymorphism method was applied in 7 of the studies. The PRISMA checklist and flowchart have been uploaded in the supplementary material, http://links.lww.com/MD/E536, http://links.lww.com/MD/E537.

3.2. Quantitative synthesis

When all of the studies pooled together (Table 2), we observed a positive correlation between the XPC Lys939Gln variant and PA susceptibility in the recessive genetic model (OR = 1.15, 95% CI = 1.02–1.30, $P_{\text{heterogeneity}} = .044$, $P = .021$, $I^2 = 45.2$). In stratified analysis by ethnicity, a considerably increased risk was also observed in Asians (OR = 1.21, 95% CI = 1.01–1.43, $P_{\text{heterogeneity}} = .008$, $P = .034$, $I^2 = 65.2$, Fig. 2). However, we found no obvious association between this polymorphism and PA risk in Caucasians (allele contrast: OR = 1.02, 95% CI = 0.93–1.11, $P_{\text{heterogeneity}} = .617$, $P = .721$, $I^2 = 0$; Gln/Gln vs Lys/Lys: OR = 1.05, 95% CI = 0.87–1.28, $P_{\text{heterogeneity}} = .658$, $P = .584$,

Table 1

Basic information of included studies for XPC Lys939Gln variant and prostate cancer risk.

First author	Year	Origin	Ethnicity	Source	Case	Control	Case CC	Case CA	Control AA	Control CC	Control CA	Control AA	HWE	Age range Case	Age range Control	Method
Hirata	2007	Japan	Asian	HB	165	165	10	78	77	23	70	72	0.372	68±5.0	67±15	PCR-RFLP
Agalliu	2010	USA	Caucasians	PB	1257	1251	205	595	457	190	600	461	0.819	NA	NA	Applied Biosystems
Agalliu	2010	USA	African	PB	147	83	16	61	70	9	38	36	0.827	NA	NA	Applied Biosystems
Mandal	2012	India	Asian	PB	192	224	28	71	93	16	94	114	0.570	62.6±8.9	59.1±10.4	PCR-RFLP
Mittal	2012	India	Asian	PB	195	250	28	73	94	19	104	127	0.727	66.0±5.46	64.7±5.71	PCR-RFLP
Liu	2012	China	Asian	HB	202	221	31	85	86	19	100	102	0.426	70.7±8.4	70.4±10.0	PCR-RFLP
Sorour	2013	Egypt	Arabian	HB	50	50	9	25	16	5	27	18	0.263	65.4±8.7	NA	PCR-RFLP
Mirecka	2014	Poland	Caucasians	PB	602	771	98	290	214	122	384	265	0.380	mean 68.3	mean 64.6	real-time PCR
Zhang	2014	China	Asian	HB	229	238	33	38	158	31	37	170	<0.001	66.7±8.2	67.3±7.5	MassARRAY
Kahnamouei	2016	Iran	Asian	HB	153	205	47	59	47	62	88	55	0.044	mean 61.7	mean 69.2	PCR-RFLP
Wang	2017	China	Asian	PB	1004	1055	131	459	414	125	495	435	0.379	NA	NA	real-time PCR
Said	2018	Tunis	African	HB	110	266	16	55	39	26	158	82	<0.001	71.8±11.3	69.0±8.51	PCR-RFLP

HB = hospital based, HWE = Hardy–Weinberg equilibrium of controls, NA = not available, PB = population based, PCR-RFLP = polymerase chain reaction and restrictive fragment length polymorphism.

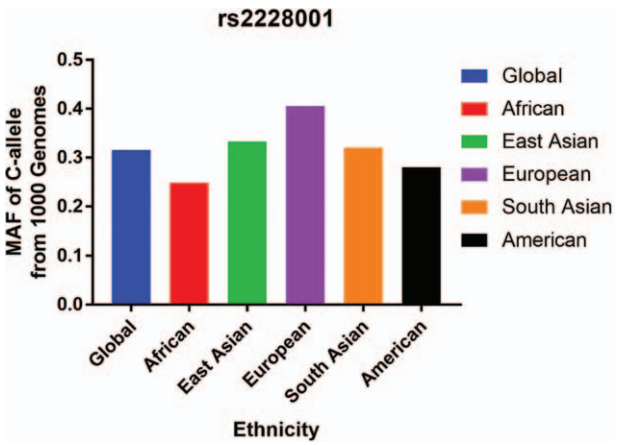

Figure 1. Minor allele and major allele frequency of xeroderma pigmentosumcomplementation group C exon15 Lys939Gln in controls stratified by race. Vertical line = allele frequency, horizontal line = allele type.

$I^2=0$; dominant genetic model: OR = 1.00, 95% CI = 0.87–1.14, $P_{heterogeneity}=.604$, $P=.953$, $I^2=0$; Gln/Gln vs Gln/Lys + Lys/Lys: OR = 1.07, 95% CI = 0.90–1.27, $P_{heterogeneity}=.783$, $P=.450$, $I^2=0$). Additionally, no positive relationship was identified in African descendants (Gln-allele vs Lys-allele: OR = 0.97, 95% CI = 0.75–1.24, $P_{heterogeneity}=.709$, $P=.785$, $I^2=0$; Gln/Gln vs Lys/Lys: OR = 1.13, 95% CI = 0.64–2.00, $P_{heterogeneity}=.560$, $P=.679$, $I^2=0$; dominant model: OR = 0.82, 95% CI = 0.58–1.18, $P_{heterogeneity}=.918$, $P=.287$, $I^2=0$; recessive model: OR = 1.32, 95% CI = 0.77–2.25 $P_{heterogeneity}=.422$, $P=.306$, $I^2=0$). Furthermore, in subgroup analysis by source of control, a notable association of this XPC polymorphism was found in population based studies (Gln/Gln vs Gln/Lys + Lys/Lys: OR = 1.15, 95% CI = 1.01–1.32, $P_{heterogeneity}=.146$, $P=.040$, $I^2=39.0$, Fig. 3). No significant correlation was demonstrated in studies using hospital based controls (Gln-allele vs Lys-allele: OR = 1.03, 95% CI = 0.90–1.18, $P_{heterogeneity}=.305$, $P=.660$, $I^2=16.8$; Gln/Gln vs Lys/Lys: OR = 1.09, 95% CI = 0.83–1.42, $P_{heterogeneity}=.062$, $P=.542$, $I^2=52.4$; dominant model: OR = 0.98, 95% CI = 0.82–1.18, $P_{heterogeneity}=.740$, $P=.858$, $I^2=0$; recessive model: OR = 1.14, 95% CI = 0.89–1.46, $P_{heterogeneity}=.037$, $P=.289$, $I^2=57.9$).

3.3. Expression of XPC utilizing in silico analysis

In silico tool evaluated expression of XPC in 497 primary tumor and 52 normal tissues. The XPC expression was lower in PA tissues than in control group ($P<.05$, Fig. 5A). Similar results were observed in Caucasian individuals ($P<.05$, Transcript per million, TPM: Caucasians vs control = 25.082 vs 29.439), but not in Africans ($P>.05$, TPM: Africans vs control = 26.424 vs 29.439, Fig. 4). Furthermore, we investigated whether XPC expression influenced the OS rate in PA cases. As described in

Table 2

Stratified analysis of XPC exon15 Lys939Gln polymorphism on prostate cancer risk.

Variables	N	Case/control	OR (95% CI) P_{heter} * P I^2 Gln-allele vs Lys-allele	OR (95% CI) P_{heter} * P I^2 Gln/Gln vs Lys/Lys	OR (95% CI) P_{heter} * P I^2 Gln/Gln + Gln/Lys vs Lys/Lys	OR (95% CI) P_{heter} * P I^2 Gln/Gln vs Gln/Lys + Lys/Lys
Total	12	4306/4779	1.04 (0.98–1.10) .516 .229 0	1.13 (0.99–1.28) .082 .068 38.8	1.00 (0.92–1.09) .971 .988 0	1.15 (1.02–1.30) .044 .021 45.2
Ethnicity						
Asian	7	2140/2358	1.06 (0.97–1.16) .208 .177 28.9	1.19 (0.99–1.43) .015 .072 62.2	1.02 (0.91–1.15) .896 .710 0	1.21 (1.01–1.43) .008 .034 65.2
Caucasian	2	1859/2022	1.02 (0.93–1.11) .617 .721 0	1.05 (0.87–1.28) .658 .584 0	1.00 (0.87–1.14) .604 .953 0	1.07 (0.90–1.27) .783 .450 0
African	2	257/349	0.97 (0.75–1.24) .709 .785 0	1.13 (0.64–2.00) .560 .679 0	0.82 (0.58–1.18) .918 .287 0	1.32 (0.77–2.25) .422 .306 0
Arabian	1	50/50	1.28 (0.73–2.26) – .387 –	2.03 (0.56–7.31) – .281 –	1.20 (0.52–2.74) – .673 –	1.98 (0.61–6.38) – 0.255 –
Source of control						
Hospital based	6	909/1145	1.03 (0.90–1.18) .305 .660 16.8	1.09 (0.83–1.42) .062 .542 52.4	0.98 (0.82–1.18) .740 .858 0	1.14 (0.89–1.46) .037 .289 57.9
Population based	6	3397/3634	1.04 (0.97–1.11) .531 .260 0	1.14 (0.99–1.32) .191 .081 32.7	1.01 (0.91–1.11) .946 .913 0	1.15 (1.01–1.32) .146 .040 39.0

CI = confidence interval, OR = odds ratio, XPC = xeroderma pigmentosumcomplementation group C.
* P value of Q test for heterogeneity test (P_{heter}).

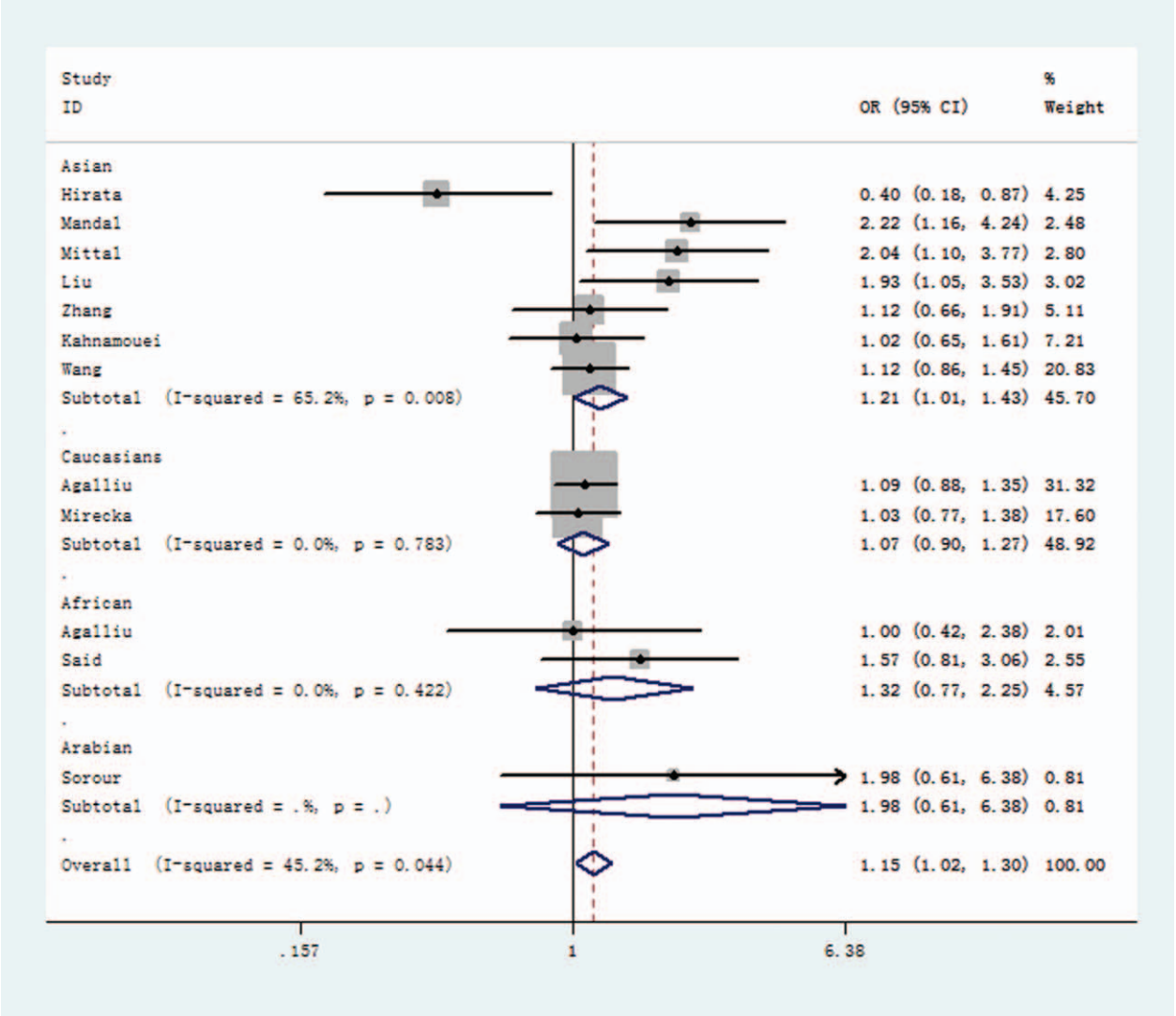

Figure 2. Forest plot of cancer risk correlated with xeroderma pigmentosumcomplementation group C exon15 Lys939Gln variant (recessive genetic model of MM vs MW + WW) in the stratified analyses by race. CI = confidence interval, OR = odds ratio.

Fig. 5B, PA subjects with high XPC expression had a longer OS time than low expression group ($P < .05$). Moreover, online database was also employed to explore the gene–gene correlation of XPC. As shown in Fig. 6A, at least 24 genes participated in the crosstalk with XPC. The ZFYVE20 gene was predicted to be the most related gene (Fig. 6B). Nevertheless, there are few studies on their connection in PA, which are required to be demonstrated in the future studies.

3.4. Publication bias

We employed Begg funnel plot to investigate publication bias in the enrolled studies. No publication bias for the XPC Lys939Gln variant was identified among all the models. For Gln-allele vs Lys-allele: $t = 0.57$, $P = .579$; Gln/Gln vs Lys/Lys: $t = 0.62$, $P = .548$; dominant genetic model: $t = 0.47$, $P = .646$; recessive genetic model: $t = 0.70$, $P = .498$. The symmetry of funnel plot also demonstrated no evidence of publication bias in the current analysis (Fig. 7).

4. Discussion

The pathogenesis of PA remains complex. Previous studies have shown that genetic variants of DNA repair genes, including XPC could downregulate the DNA repair capacity.[12,31] Decreased DNA repair capacity causes genetic instability and could contribute to PA susceptibility.[32,33] Up to now, various case–control studies were carried out to evaluate whether the XPC exon15 Lys939Gln polymorphism confer individual's PA risk. Nevertheless, previous studies have shown controversial results.[16–22] A previous study based on Japanese population suggested that XPC Lys939Gln variant might be a risk factor for PA susceptibility.[16] However, another study indicated no significant difference in the XPC Lys939Gln genotypes of PA participants and control subjects in Egyptian populations.[21] In 2013, He et al carried out a meta-analysis and demonstrated an elevated colorectal, lung, and bladder cancer susceptibility associated with this variant, especially in Asian population.[34] Two years later, another study showed no statistical difference

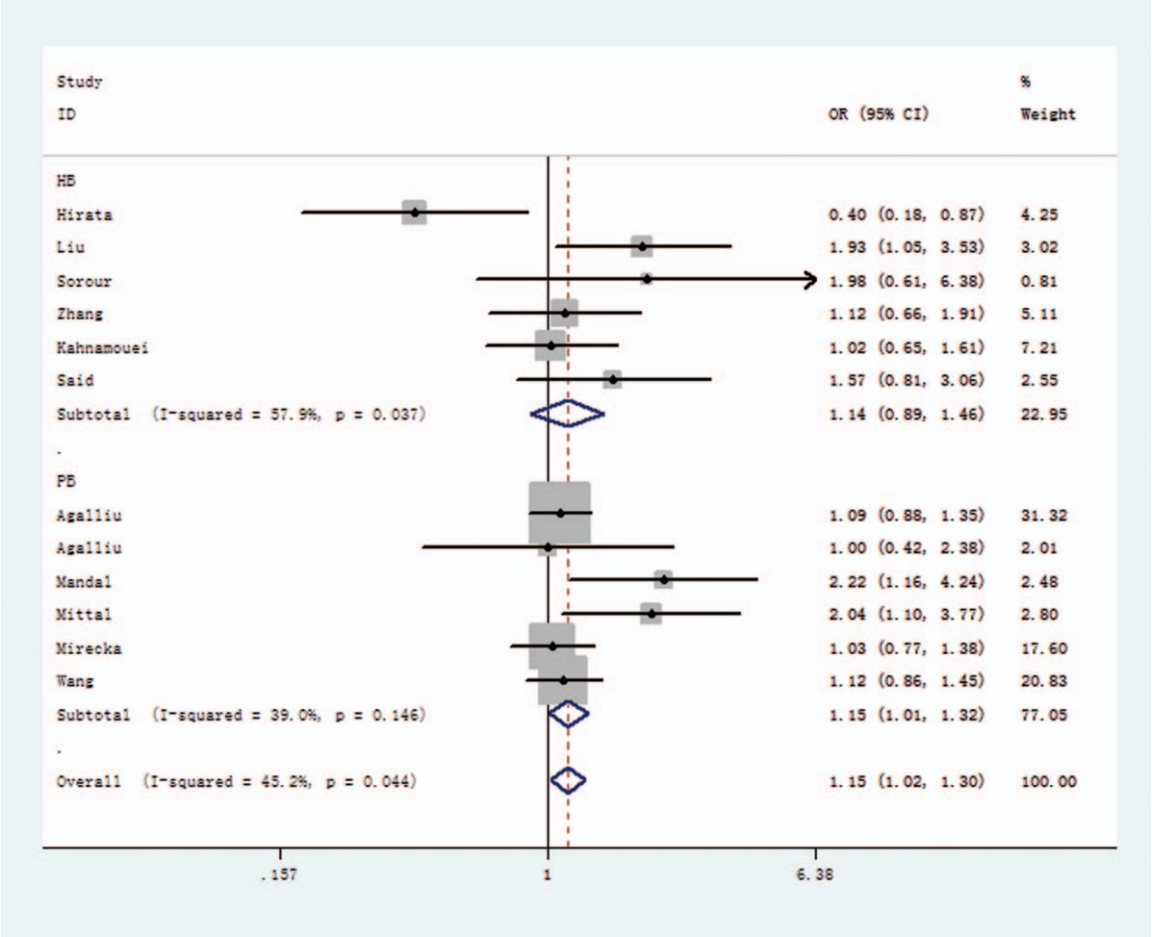

Figure 3. Forest plot of MM vs MW + WW genetic model of xeroderma pigmentosumcomplementation group C exon15 Lys939Gln polymorphism in subgroup analyses by source of control. CI = confidence interval, OR = odds ratio.

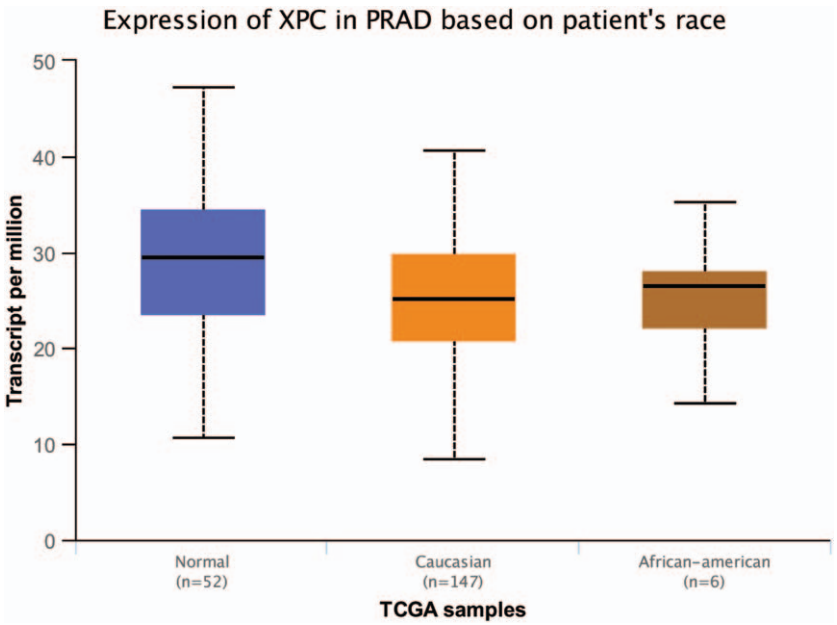

Figure 4. Association of xeroderma pigmentosumcomplementation group C expression based on sample types (A) and the overall survival probability (B) among prostate adenocarcinoma participants.

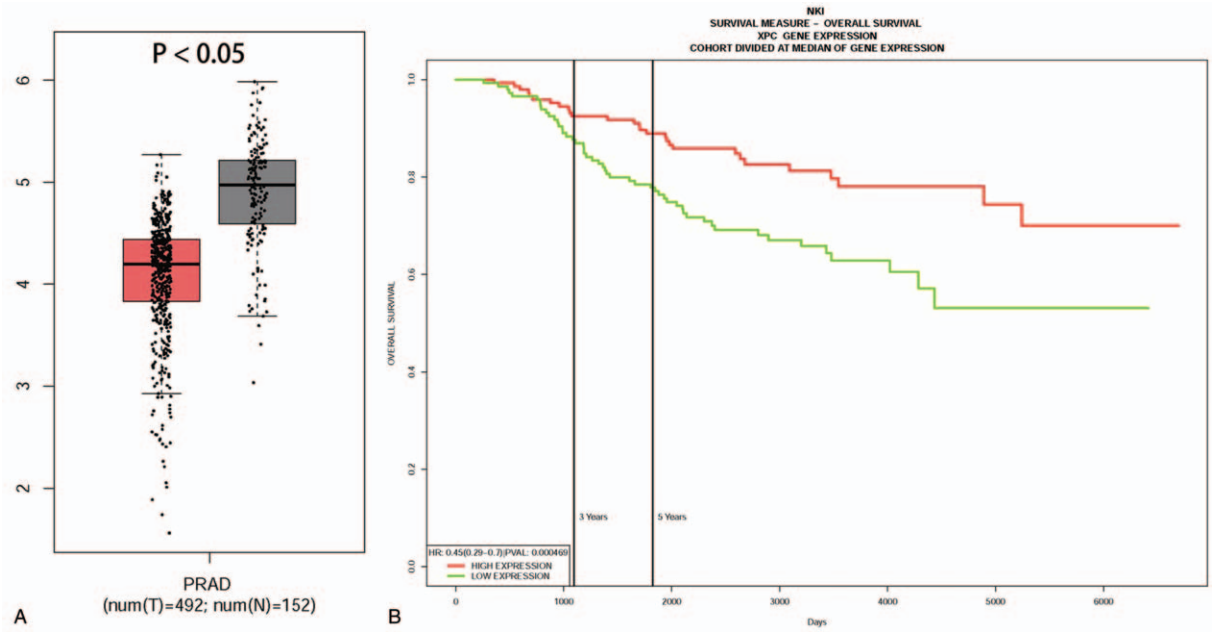

Figure 5. In silico analysis of xeroderma pigmentosumcomplementation group C (XPC) expression in prostate adenocarcinoma participants based on patients' race. PRAD = prostate adenocarcinoma, TCGA = The Cancer Genome Atlas.

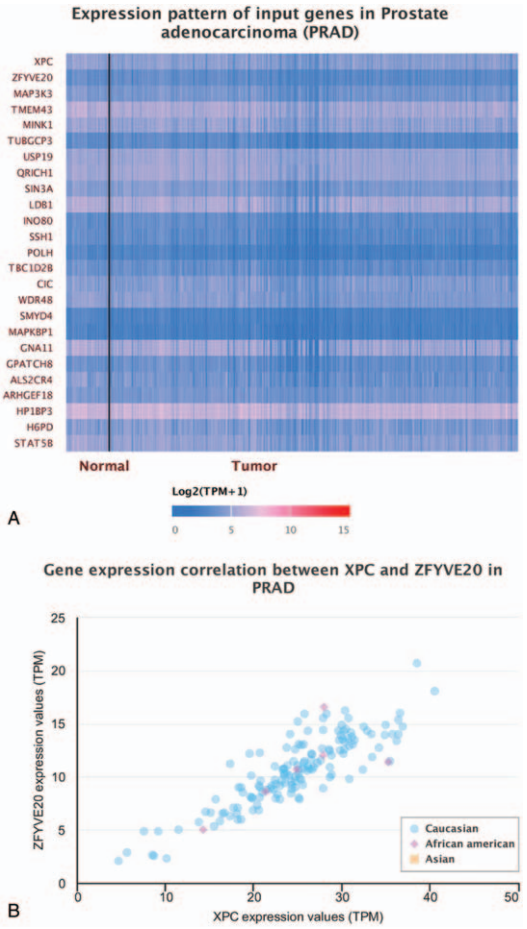

Figure 6. Xeroderma pigmentosumcomplementation group C (XPC) correlations crosstalk with other gene. At least 24 genes were involved in the interaction of XPC (A). The ZFYVE20 gene was the most related gene (B).

between XPC Lys939Gln polymorphism and PA risk.[35] With the emergence of new case–control studies, the current study aimed to summarize all eligible data to achieve more accurate conclusions.

In this study, a total of 4306 cases and 4779 control subjects were investigated to determine the role of XPC Lys939Gln variant in PA susceptibility. We found a statistically increased risk of PA in the overall analysis (OR = 1.15, 95% CI = 1.02–1.30, $P = .021$). In subgroup analysis by ethnicity, we observed a significantly elevated risk in Asian populations (OR = 1.21, 95% CI = 1.01–1.43, $P = .034$). A similar positive finding was obtained in studies using population based controls (OR = 1.15, 95% CI = 1.01–1.32, $P = .040$), in line with the results reported by He et al.[34] Furthermore, in silico analysis evaluated the expression of XPC in Caucasian and African participants and showed evidence that XPC expression was downregulated in Caucasian PA tissues compared to control subjects. However, no statistical difference was identified in African descendants. Although large amounts of resources have been invested to determine the basis of genetic susceptibility to PA, the development of genomic biomarkers that can be used to predict PA susceptibility has only recently begun to gain traction. In this case, several studies using metabolomics and proteomics techniques were conducted to investigate potential biomarkers for PA.[36–39] We evaluated whether the XPC expression influenced the OS probability of PA cases, which show evidence that PA subjects with high XPC expression had a longer OS time than low expression group. It is possible that the prognosis of PA could be predicted by testing the expression of XPC in PA patients.

Meta-analysis is a type of retrospective study that can be influenced by methodologic deficiencies of the enrolled studies, and some limitations should be mentioned. First, the number of included studies in our study remains small, especially for subgroup analyses. Second, some covariates and risk factors including age, tumor grade, and smoking status should be assessed to obtain more accurate results. We tried to further

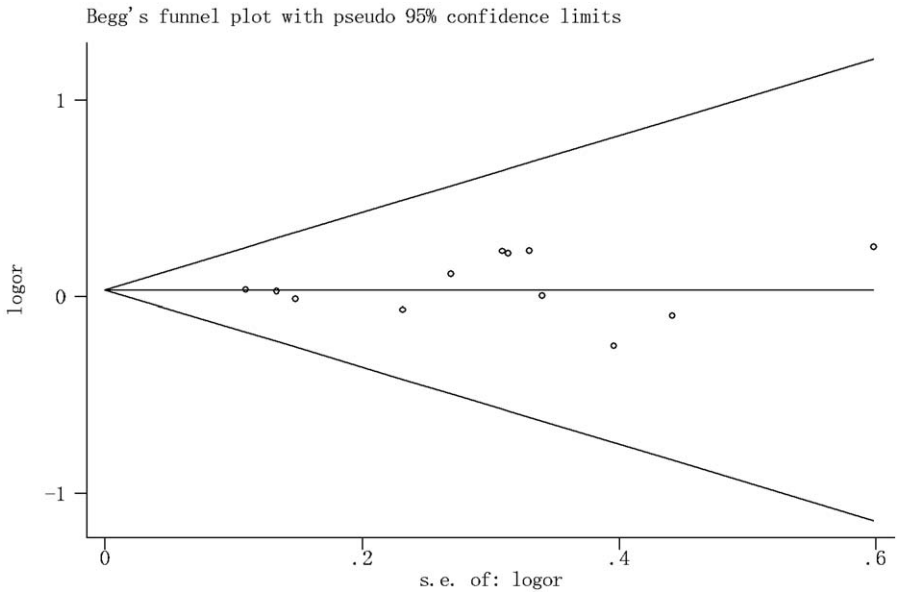

Figure 7. Begg funnel plot of publication bias for xeroderma pigmentosumcomplementation group C exon15 Lys939Gln variant under recessive model.

evaluate the correlation between XPC Lys939Gln polymorphism and these factors; nevertheless, lacking of original data in the enrolled publications might have influenced the ultimate assessment. Last but not least, other factors such as gene–gene and variant–variant interactions should be considered. Said et al reported that XPC Lys939Gln variant was not associated with PA risk; however, combined analysis of Lys939Gln and XPC-PAT polymorphism indicated that individuals carrying XPC (Lys/Gln + PAT D/D) genotypes were associated with PA susceptibility compared to controls.[26] On the contrary, our analysis has also some advantages. First, all eligible studies based on inclusion criteria were selected to assess the relationship between XPC Lys939Gln polymorphism and PA susceptibility. Hence, statistical power of the present analysis was strengthened. Second, Begg funnel plot showed no evidence of publication bias, indicating that conclusions from the above analyses were solid and trustworthy.

5. Conclusions

The present study suggested that XPC Lys939Gln variant might contribute to increased PA susceptibility, especially for Asian descendants. Similar findings were also obtained in population-based studies. XPC might be related to the prognosis of PA. Future large scale and well-designed studies with different ethnic descendants are necessary to validate our findings.

Author contributions

FQ and LZ contributed to the study design, LFZ, SLG and LS extracted the data, KX and LS drafted the manuscript, LFZ and ZZ prepared figures and tables, ZZ, QXS and LJZ revised the manuscript. All authors approved the final manuscript.

References

[1] Bray F, Lortet-Tieulent J, Ferlay J, et al. Prostate cancer incidence and mortality trends in 37 European countries: an overview. Eur J Cancer 2010;46:3040–52.
[2] Jemal A, Siegel R, Xu J, et al. Cancer statistics, 2010. CA Cancer J Clin 2010;60:277–300.
[3] McCracken M, Olsen M, Chen MSJr, et al. Cancer incidence, mortality, and associated risk factors among Asian Americans of Chinese, Filipino, Vietnamese, Korean, and Japanese ethnicities. CA Cancer J Clin 2007;57:190–205.
[4] Akaza H, Onozawa M, Hinotsu S. Prostate cancer trends in Asia. World J Urol 2017;35:859–65.
[5] Abidi SH, Bilwani F, Ghias K, et al. Viral etiology of prostate cancer: genetic alterations and immune response. A literature review. Int J Surg 2018;52:136–40.
[6] Halperin R, Maas B, Pickles T. Complications of prostate cancer treatment. Lancet Oncol 2014;15:e151–2.
[7] Malins DC, Johnson PM, Wheeler TM, et al. Age-related radical-induced DNA damage is linked to prostate cancer. Cancer Res 2001;61:6025–8.
[8] Chen ZP, Malapetsa A, Monks A, et al. Nucleotide excision repair protein levels vis-à-vis anticancer drug resistance in 60 human tumor cell lines. Ai Zheng 2002;21:233–9.
[9] Thoma BS, Vasquez KM. Critical DNA damage recognition functions of XPC-hHR23B and XPA-RPA in nucleotide excision repair. Mol Carcinog 2003;38:1–3.
[10] Hoogstraten D, Bergink S, Ng JM, et al. Versatile DNA damage detection by the global genome nucleotide excision repair protein XPC. J Cell Sci 2008;121:2850–9.
[11] Khan SG, Metter EJ, Tarone RE, et al. A new xeroderma pigmentosum group C poly(AT) insertion/deletion polymorphism. Carcinogenesis 2000;21:1821–5.
[12] Qiu L, Wang Z, Shi X, et al. Associations between XPC polymorphisms and risk of cancers: a meta-analysis. Eur J Cancer 2008;44:2241–53.
[13] Sun HY, Zuo L, Zou JG, et al. Current evidence on XPC rs2228001A/C polymorphism and bladder cancer susceptibility. Int J Clin Exp Med 2016;9:2881–8.
[14] Peng Q, Lao X, Tang W, et al. XPC Lys939Gln polymorphism contributes to colorectal cancer susceptibility: evidence from a meta-analysis. Diagn Pathol 2014;9:120.
[15] Zhu ML, Hua RX, Zheng L. Associations between polymorphisms of the XPC gene and lung cancer susceptibility: a meta-analysis. Tumour Biol 2014;35:2931–9.
[16] Hirata H, Hinoda Y, Tanaka Y, et al. Polymorphisms of DNA repair genes are risk factors for prostate cancer. Eur J Cancer 2007;43:231–7.
[17] Agalliu I, Kwon EM, Salinas CA, et al. Genetic variation in DNA repair genes and prostate cancer risk: results from a population-based study. Cancer Causes Control 2010;21:289–300.
[18] Liu Y, Chen Z, Wei Q, et al. Poly (AT) polymorphism in the XPC gene and smoking enhance the risk of prostate cancer in a low-risk Chinese population. Cancer Genet 2012;205:205–11.

[19] Mandal RK, Gangwar R, Kapoor R, et al. Polymorphisms in base-excision & nucleotide-excision repair genes & prostate cancer risk in north Indian population. Indian J Med Res 2012;135:64–71.
[20] Mittal RD, Mandal RK. Genetic variation in nucleotide excision repair pathway genes influence prostate and bladder cancer susceptibility in North Indian population. Indian J Hum Genet 2012;18:47–55.
[21] Sorour AF, Talaat IM, Youssif TMA, et al. Detection of polymorphisms of DNA repair genes (XRCC1 and XPC) in prostate cancer. J Cancer Therapy 2013;4:1499–505.
[22] Mirecka A, Paszkowska-Szczur K, Scott RJ, et al. Common variants of xeroderma pigmentosum genes and prostate cancer risk. Gene 2014; 546:156–61.
[23] Zhang XJ, Liu P, Zhu F. Polymorphisms of DNA repair-related genes with susceptibility and prognosis of prostate cancer. Genet Mol Res 2014;13:4419–24.
[24] Kahnamouei SA, Narouie B, Sotoudeh M, et al. Association of XPC gene polymorphisms with prostate cancer risk. Clin Lab 2016;62:1009–15.
[25] Wang M, Li Q, Gu C, et al. Polymorphisms in nucleotide excision repair genes and risk of primary prostate cancer in Chinese Han populations. Oncotarget 2017;8:24362–71.
[26] Said R, Bougatef K, Setti Boubaker N, et al. Polymorphisms in XPC gene and risk for prostate cancer. Mol Biol Rep 2019;46:1117–25.
[27] Barili F, Parolari A, Kappetein PA, et al. Statistical Primer: heterogeneity, random- or fixed-effects model analyses? Interact Cardiovasc Thorac Surg 2018;27:317–21.
[28] Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 1959;22:719–48.
[29] Tang Z, Li C, Zhang K, et al. GE-mini: a mobile APP for large-scale gene expression visualization. Bioinformatics 2017;33:941–3.
[30] Yang B, Chen WH, Wen XF, et al. Role of DNA repair-related gene polymorphisms in susceptibility to risk of prostate cancer. Asian Pac J Cancer Prev 2013;14:5839–42.
[31] Jin B, Dong Y, Zhang X, et al. Association of XPC polymorphisms and lung cancer risk: a meta-analysis. PLoS One 2014;9:e93937.
[32] Park JY, Huang Y, Sellers TA. Single nucleotide polymorphisms in DNA repair genes and prostate cancer risk. Methods Mol Biol 2009;471:361–85.
[33] Lockett KL, Snowhite IV, Hu JJ. Nucleotide-excision repair and prostate cancer risk. Cancer Lett 2005;220:125–35.
[34] He J, Shi TY, Zhu ML, et al. Associations of Lys939Gln and Ala499Val polymorphisms of the XPC gene with cancer susceptibility: a meta-analysis. Int J Cancer 2013;133:1765–75.
[35] Wu H, Lv Z, Wang X, et al. Lack of association between XPC Lys939Gln polymorphism and prostate cancer risk: an updated meta-analysis based on 3039 cases and 3253 controls. Int J Clin Exp Med 2015; 8:17959–67.
[36] De Cobelli O, Buonerba C, Terracciano D, et al. Urotensin II receptor on preoperative biopsy is associated with upstaging and upgrading in prostate cancer. Future Oncol 2015;11:3091–8.
[37] Gabriele C, Cantiello F, Nicastri A, et al. High-throughput detection of low abundance sialylated glycoproteins in human serum by TiO2 enrichment and targeted LC-MS/MS analysis: application to a prostate cancer sample set. Anal Bioanal Chem 2019;411:755–63.
[38] Lucarelli G, Loizzo D, Ferro M, et al. Metabolomic profiling for the identification of novel diagnostic markers and therapeutic targets in prostate cancer: an update. Expert Rev Mol Diagn 2019;19:377–87.
[39] Ferro M, Buonerba C, Terracciano D, et al. Biomarkers in localized prostate cancer. Future Oncol 2016;12:399–411.