CYP1A1 Polymorphisms and Risk of Prostate Cancer
A Meta-analysis

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Introduction: Two common polymorphisms in cytochrome P450; family 1, subfamily A, polypeptide 1 (*CYP1A1*); have been implicated as a risk factor of prostate cancer, but individual studies have been inconclusive or controversial. We reviewed studies on *CYP1A1* polymorphisms in patients with prostate cancer.

Materials and Methods: The strategy searching in the PubMed was based on combinations of *prostate cancer*, *CYP1A1*, *CYP1A1 gene polymorphism*, and *genetic susceptibility*. The last search update was May 2008. The retrieved articles and their bibliographies of were evaluated and reviewed independently by 2 experts. We shortlisted 19 studies, of which 14 on sporadic prostate cancer were analyzed. Overall, 2573 patients with prostate cancer and 2576 controls were analyzed.

Results: The random effects odds ratio was 1.350 (95% confidence interval, 1.110 to 1.641; P = .003) for T/C polymorphism and 1.085 (95% confidence interval, 0.863 to 1.364; P = .49) for A/G polymorphism. The A/G polymorphism was not associated with increased risk of prostate cancer. However, the T/C polymorphism showed conflicting results in different studies, while overall, this polymorphism showed significant effects on the susceptibility to prostate cancer. There was no significant between-study heterogeneity for both polymorphisms with respect to distribution of alleles.

Conclusion: This meta-analysis suggests that while the *CYP1A1* T/C polymorphism is likely to considerably increase the risk of sporadic prostate cancer on a wide population basis, the A/G polymorphism may not influence this risk. However, the association of polymorphisms may be significant with respect to smoking history, diet habits, ethnicity, and race.

Keywords: prostatic neoplasms, meta-analysis, CYP1A1, genetic polymorphisms

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INTRODUCTION

Prostate cancer is one of the most common malignancies in men, and the prostate is the leading site for cancer incidences, accounting for 31% of new cancer cases in men.[1] The incidence of prostate cancer varies greatly with race and geography. In India, the annual mortality in 2000 was 700 000, and the annual estimate of cancer for the year 2001 was 980 000. It is relatively rare for prostate cancer to be diagnosed in men younger than 50 years old, but above this age, the incidence and mortality rates increase exponentially.[1,2] Genetic susceptibility to prostate cancer is an important research area, especially since the incidence of prostate cancer has been rapidly increasing. Prostate cancer susceptibility loci have been reported to be hereditary prostate cancer 1 gene at 1q24,

predisposing for prostate cancer gene at 1q42, X-linked hereditary prostate cancer gene at Xq27, capsule biosynthesis protein gene at 1p36, and hereditary prostate cancer 20 gene at 20q13.[2]

The association of prostate cancer with polymorphisms of common variants in genes involved in steroid hormone metabolism including androgen receptor (*AR*), steroid-5-alpha-reductase, alpha polypeptide 2, cytochrome P450 subfamily XVII, vitamin D receptor, etc, have been extensively examined.[3-7] Cytochrome P450, family 1, subfamily A, polypeptide 1 (*CYP1A1*) is involved in xenobiotic metabolism and classified as a phase I enzyme. The expression of the *CYP1A1* is induced in a ligand-dependent fashion by the aryl hydrocarbon receptor and aryl hydrocarbon receptor nuclear translocator.[1,2,8] The *CYP1A1* gene plays an important role in carcinogenesis of various cancers, and it might affect carcinogenesis of prostate cancer through alteration of genotoxicity and hormone imbalance. It is inhibited by fluoroquinolones and macrolides, induced by aromatic hydrocarbons. There are 3 main subtypes of CYP1A: M1, M2, and M3. *CYP1A1* and *CYP1B1* are regulated by the aryl hydrocarbon receptor, a ligand-activated transcription factor which is a part of the phase I reactions in drug metabolism.[8]

Current published evidence suggests that both environmental and genetic factors influence the pathogenesis of prostate cancer.[9,10] Polymorphisms of the *CYP1A1* may modify the risk for prostate cancer.[8,9] The *CYP1A1* gene encodes a phase I cytochrome, P-450 enzyme, that converts environmental procarcinogens to reactive intermediates having carcinogenic effects.[11] In addition, *CYP1A1* is involved in the oxidative metabolism of estrogens, which may play a critical role in the etiology of prostate cancer.[12] Two common polymorphisms in *CYP1A1* have been reported: one is a T/C substitution located 264 bp downstream from the 3'-flanking region, forming an Msp1 restriction site (*CYP1A1m1*); the second is a G/A substitution at the 4889 bp position of exon 7, which leads to an amino acid substitution (Ile to Val) of its protein (*CYP1A1m2*).[1,13] The association of these *CYP1A1* single nucleotide polymorphisms (SNPs) with cancer (eg, lung, oesophageal, breast, oral cavity cancers) has been well documented.[1,14] More recently, the association between *CYP1A1* SNPs and prostate cancer has been reported in some groups.[13]

Molecular epidemiological studies have presented seemingly contradictory results concerning the potential role of the *CYP1A1* polymorphisms in prostate cancer susceptibility. Using relevant accumulated data, a quantitative methodology was used to estimate the strength of *CYP1A1* genetic associations.

MATERIALS AND METHODS

Identification of Relevant Studies

We considered all studies that examined the association of the *CYP1A1* gene polymorphisms with prostate cancer. We shortlisted 19 studies, of which 14 were analyzed further. Results of only sporadic prostate cancer were considered for meta-analyses. We excluded studies with familial linkage designs. All of the obtained studies (familial and sporadic) were tabulated to have an overview of the number of studies carried out in prostate cancer which used *CYP1A1* gene for analyses. Search sources included MEDLINE which was searched through PubMed. The last search update was May 2008. The search strategy was based on combinations of *prostate cancer*, *CYP1A1*, *CYP1A1 gene polymorphism*, and *genetic susceptibility*. The retrieved articles and their bibliographies of were evaluated and reviewed independently by 2 experts. Case-control studies were eligible if they had determined the distribution of *CYP1A1* genotypes in prostate cancer cases and in a concurrent control group of prostate cancer-free subjects using a molecular method for genotyping. We accepted disease-free controls regardless of whether they had benign prostatic hyperplasia or did not. Cases with prostate cancer were eligible regardless of whether they had a first-degree relative with prostate cancer or not. However, we excluded hereditary prostate cancer results from 2 family-based studies.[15,16]

Data Extraction

The following information was sought from

extracted data: authors, journal and year of publication, country of origin, selection and characteristics of prostate cancer cases and controls, demographics, racial descent of the study population, eligible and genotyped cases and controls, and number of cases and controls for each *CYP1A1* genotype.

Meta-analysis

The primary analysis for all *CYP1A1* gene polymorphisms was based on distribution of genotypes among various populations, and then, evaluation of the overall differences within them. We also examined the contrast of the two groups of homozygotes (the dominant and recessive). The odds ratio (OR) was used for analyses of results. For each genetic contrast, we estimated the between-study heterogeneity across all eligible comparisons, using the modified chi-square test. Heterogeneity was considered significant is *P* value was less than .05. All analyses were conducted using the Comprehensive Meta-Analysis Software version 2 (Biostat, Englewood, New Jersey, USA).

RESULTS

Eligible Studies

Fourteen studies probing the relationship between the *CYP1A1* gene polymorphism and prostate cancer susceptibility were identified.[15-28] Two studies by Chang and colleagues and Cunningham and coworkers[15,16] also included a family-based history; therefore, the data of only sporadic prostate cancer cases were collected (Table 1). Most of the studies had selected patients with prostate cancer based on a histological diagnosis from biopsy and/or prostatectomy. In 1 study by Nock and coleagues,[17] controls were unaffected brothers of the patients with prostate cancer. Controls did not have a clinical diagnosis of prostate cancer, confirmed using additional screening (with digital rectal examination, prostate specific antigen [PSA $<$ 4 ng/mL], and needle biopsy or prostate resection; Table 1). A few investigators had also matched their groups for smoking status and alcoholism in relation to risk of prostate cancer. Molecular methods for genotyping were checked. All studies had used polymerase chain reaction assay, and 3 studies had also used sequencing.

Meta-analysis

The selected studies included a total of 5832 subjects (2766 patients and 3066 controls) while the eligible subjects were 2573 patients and 2576 controls. Allele and genotype frequencies per

Table 1. Characteristics of the Study Population in Selected Studies Included in Meta-analyses

Study	Population	Samples		Age of Studied Population, y	
		Patients	Controls	Patients	Controls
Chang et al, 2003[15]	Caucasians and African-Americans	159 familial and 245 sporadic	222*	Mean, 61.0 for familial and 58.7 for sporadic	Mean, 58
Beer et al, 2002[18]	Caucasians	117	183	≥ 18	≥ 18
Atkas et al, 2004[19]	Turkish	100	107†	Mean, 68.2 (49 to 86)	Mean, 67.8 (43 to 87)
Mittal and Srivastava, 2007[20]	Indian	130	140	Mean, 62.5	Mean, 58.5
Li, 2008[21]	Chinese	208	230	Median, 72.0 (46 to 94)	Median, 67 (45 to 81)
Cunningham et al, 2007[16]	Hispanic, Caucasian, and African-American	438 familial and 499 sporadic	493	45 to 89	45 to 89
Yang et al, 2006[22]	South Chinese	225	250	Mean, 71.6	Mean, 71.0
Nock et al, 2006[17]	Caucasians, African-Americans, and Asians	439	479‡	Mean, 61.5	Mean, 62.8
Silig et al, 2006[23]	Turkish	152	169	50 to 85	49 to 88
Caceres et al, 2005[26]	Chilean	103	132	Mean, 68.7	Mean, 63.3
Figer et al, 2003[27]	Israeli	224	250	Mean, 64.6 (45 to 81)	Mean, 61.7 (35 to 83)
Murata et al, 2001[28]	Japanese	115	204	Mean, 73.0	Mean, 71.2
Suzuki et al, 2003[24]	Japanese	81	105	Mean, 70.6 (40 to 88)	Mean, 71.2 (51 to 88)
Acevedo et al, 2003[25]	Chilean	128	102†	Mean, 68.6	Mean, 63.4

*Of the controls, 5.6% had brothers or a father affected with prostate cancer.
†The controls were men with benign prostatic hyperplasia.
‡The controls were unaffected brothers of the patients with prostate cancer.

group are shown in Tables 2 and 3. Some other studies not included in the meta-analysis but found relevant are presented in Table 4.[9,16,17,27-31] The T allele was the most highly represented among controls and cases of all studies irrespective of the descent. Overall, the prevalence of TT, TC, and CC genotypes was 52.6%, 67.7%, and 20.6% in the control individuals and 48.0%, 61.2%, and 13.9% in the patients with prostate cancer. For the Ile/Val polymorphism, the prevalence of AA, AG, and GG genotypes was 66.6%, 26.8%, and 6.4% in the controls and 64.3%, 28.8%, and 6.7% in the patients. The distribution of genotypes in both of the groups was consistent with Hardy-Weinberg equilibrium in all studies.

Table 2. Distribution of *CYP1A1* MspI Polymorphism in Various Populations

Genotype (MspI) in Studies	Patients	
	Prostate Cancer	Controls
Chang et al, 2003[15]		
TT	188 (83.9)	135 (75.0)
TC	36 (16.1)	39 (21.7)
CC	0	6 (3.3)
Mittal and Srivastava, 2007[20]		
TT	55 (42.3)	75 (53.6)
TC	69 (53.1)	58 (41.4)
CC	6 (4.6)	7 (5.0)
Li, 2008[21]		
TT	78 (37.5)	102 (44.4)
TC	100 (48.1)	84 (36.5)
CC	30 (14.4)	44 (19.1)
Yang et al, 2006[22]		
TT	76 (33.8)	96 (38.4)
TC	116 (51.6)	112 (44.8)
CC	33 (14.7)	42 (16.8)
Silig et al, 2006[23]		
TT + TC	142 (94.0)	153 (90.0)
CC	10 (6.0)	16 (10.0)
Caceres et al, 2005[26]		
TT	39 (38.2)	74 (56.2)
TC	50 (48.0)	47 (35.4)
CC	14 (13.8)	11 (8.4)
Murata et al, 2001[28]		
TT	60 (52.2)	118 (59.0)
TC	49 (42.6)	74 (37.0)
CC	6 (5.2)	8 (4.0)
Suzuki et al, 2003[24]		
TT	46 (35.8)	46 (43.8)
TC	39 (48.1)	37 (35.2)
CC	13 (16.0)	22 (21)
Acevedo et al, 2003[25]		
TT	39 (38.2)	72 (56.2)
TC	49 (48.0)	45 (35.1)
CC	14 (13.7)	11 (8.5)

Table 3. Distribution of *CYP1A1* Ile/Val Polymorphism in Various Populations

Genotype (Ile/Val) in Studies	Patients	
	Prostate Cancer	Controls
Chang et al, 2003[15]		
AA	210 (93.8)	162 (90.0)
AG	14 (16.1)	18 (10.0)
GG	0	0
Beer et al, 2002[18]		
AA	101 (91.8)	129 (88.3)
AG	7 (6.4)	17 (11.6)
GG	2 (1.2)	0
Atkas et al, 2004[19]		
AA	41 (41.0)	50 (46.7)
AG	45 (45.0)	51 (47.7)
GG	14 (14.0)	6 (5.6)
Li, 2008[21]		
AA	120 (57.7)	150 (65.2)
AG	75 (36.1)	66 (28.7)
GG	13 (6.2)	14 (6.1)
Yang et al, 2006[22]		
AA	113 (50.2)	151 (60.4)
AG	90 (40.0)	86 (34.4)
GG	22 (9.8)	13 (5.2)
Murata et al, 2001[28]		
AA	60 (52.2)	125 (62.5)
AG	42 (36.5)	64 (32.0)
GG	13 (11.3)	11 (5.5)
Suzuki et al, 2003[24]		
AA	39 (48.1)	65 (61.9)
AG	34 (42.0)	33 (31.4)
GG	8 (9.9)	7 (6.7)

Overall Effects for Alleles

The T/C polymorphism was associated with increased risk of prostate cancer (summary random effects OR, 1.350; 95% confidence interval [CI], 1.110 to 1.641; $P = .003$; Figure 1). No association was found between A/G polymorphism with prostate cancer .The summary random effects OR for G/A polymorphism was 1.085 (95% CI, 0.863 to 1.364; $P = .49$; Figure 2). However, there was no significant heterogeneity between the 14 study comparisons for both polymorphisms with respect to distribution of alleles. The Q-value for T/C polymorphism was 9.799 ($I^2 = 28.561$; $P = .20$; Table 5), while for A/G polymorphism, it was 7.968 ($I^2 = 24.702$; $P = .24$; Table 6). To assess the publication bias among the selected

Table 4. Results of *CYP1A1* Polymorphisms in Some Additional Studies*

Study	Population	Samples		Studied Genotype	Age, y		Interpretation
		Patients	Controls		Patients	Controls	
Cunningham et al, 2007[16]	Hispanic, Caucasian, and African-American	499	493	SNP analysis	45 to 89	45 to 89	No significant association
Nock et al, 2006[17]	Asians, Caucasian, and African-American	439	479	*CYP1A1* (Ile/val)	Mean, 61.5	Mean, 62.8	No significant association
Nock et al, 2007[31]	Asians, Caucasian, and African-American	637	244	*CYP1A1* (Ile/val)	Mean, 60.8	Mean, 71.6	No significant association
Figer et al, 2003[27]		224	250	*CYP1A1* (Ile/val)	Mean, 64.6	Mean, 61.7	No significant association
Gao et al, 2003[9]	Chinese	48	112	*CYP1A1* (Ile/val)	…	…	A/G associated with PC risk
Murata et al, 1998[28]	Japanese	115	204	*CYP1A1* (MspI) *CYP1A1* (Ile/Val)	Mean, 73	Mean, 71	Ile/Val and Val/Val associated with PC risk
Guan et al, 2005[30]	Chinese	83	115	Gene Chip Technique	…	…	No significant association
Vijayalakshmi et al, 2005[29]	South Indian	100	100	*CYP1A1* (MspI) *CYP1A1* (Ile/Val)	…	…	T/C associated with increased risk, A/G associated with decreased risk of PC

*SNP indicates single nucleotide polymorphism; *CYP1A1*, cytochrome P450, family 1, subfamily A, polypeptide 1; and PC, prostate cancer.

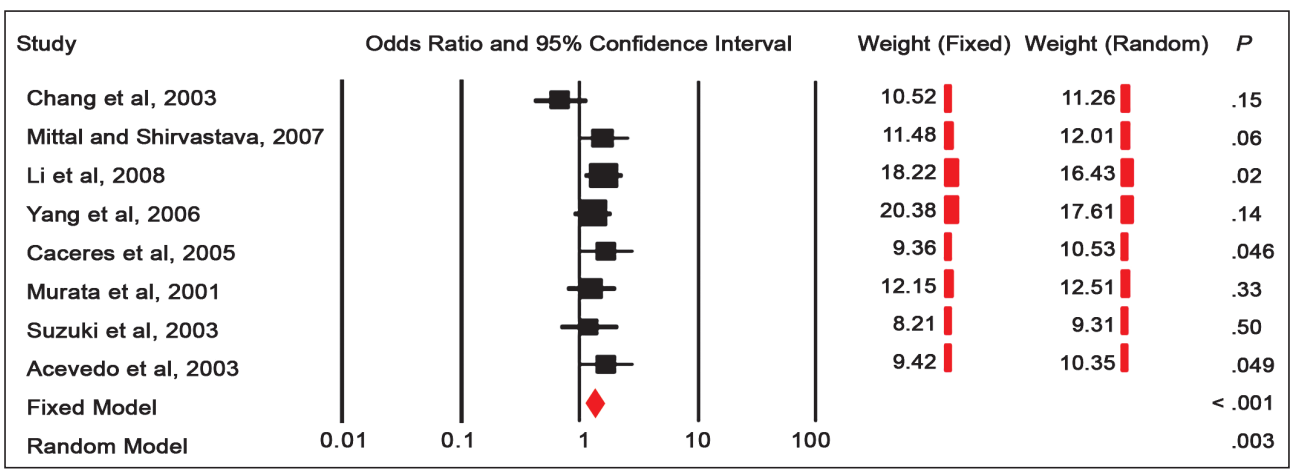

Figure 1. Odds ratio and 95% confidence interval of the distribution of *CYP1A1* MspI polymorphism (TC genotype).

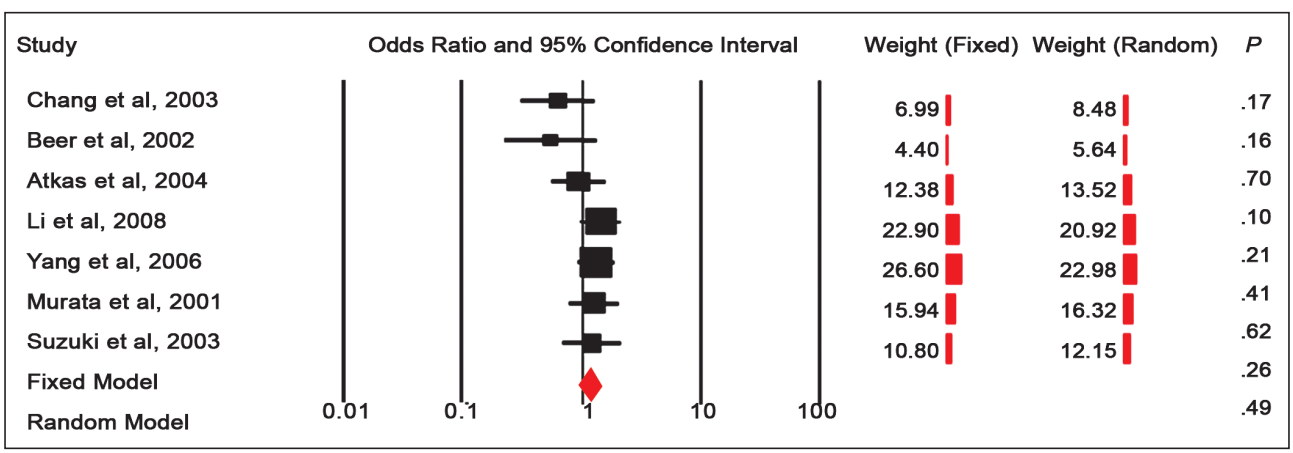

Figure 2. Odds ratio and 95% confidence interval of the distribution of *CYP1A1* Ile/Val polymorphism (AG genotype).

Table 5. Heterogeneity Between Study Populations Assessed for *CYP1A1* MspI Polymorphism (TC Genotype)*

Model	Number of Studies	Effect Size and 95% Confidence Interval			Test of Null (2-Tail)		heterogeneity			
		Point Estimate	Lower Limit	Upper Limit	Z	*P*	Q	df(Q)	*P*	I-Squared
Fixed	8	1.354	1.150	1.594	3.645	< .001	9.799	7	.20	28.561
Random	8	1.350	1.110	1.641	3.007	.003	…	…	…	…

*Ellipses indicate not applicable.

Table 6. Heterogeneity Between Study Populations Assessed for *CYP1A1* Ile/Val Polymorphism (AG Genotype)

Model	Number of Studies	Effect Size and 95% Confidence Interval			Test of Null (2-Tail)		heterogeneity			
		Point Estimate	Lower Limit	Upper Limit	Z	*P*	Q	df(Q)	*P*	I-Squared
Fixed	7	1.117	0.922	1.354	1.130	.26	7.968	6	.24	24.702
Random	7	1.085	0.863	1.364	0.696	.49	…	…	…	…

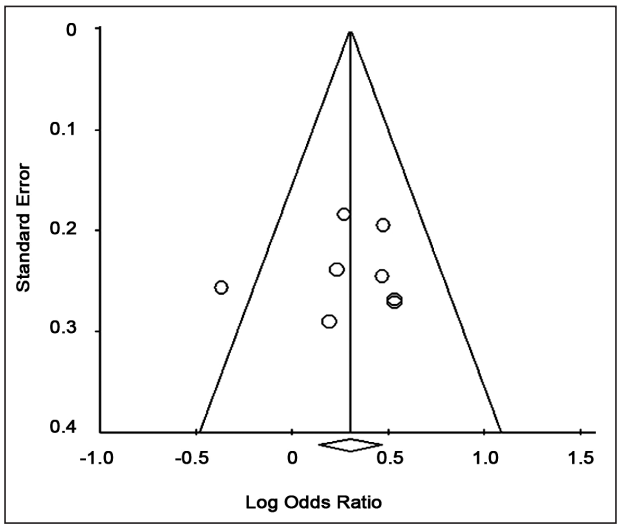

Figure 3. Funnel plot to estimate the amount of publication bias in studies on *CYP1A1* MspI polymorphism (TC genotype).

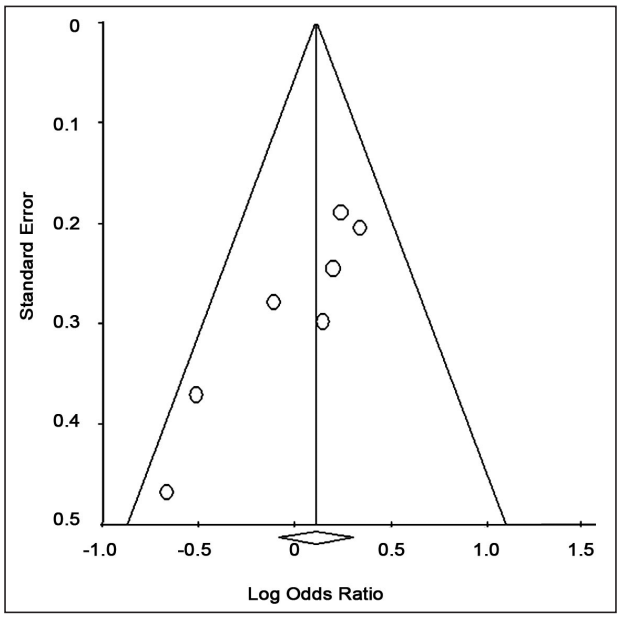

Figure 4. Funnel plot to estimate the amount of publication bias in studies on *CYP1A1* Ile/Val polymorphism (AG genotype).

studies, Funnel plots were constructed for both T/C and A/G polymorphisms (Figures 3 and 4).

DISCUSSION

CYP1A1 is likely to play an important role in the etiology of prostate cancer through its function in activating environmental procarcinogens and catalyzing the oxidative metabolites of estrogens. To test the hypothesis that genetic polymorphisms in the *CYP1A1* gene may be associated with the risk of prostate cancer, studies have been performed in various populations. In Chinese men,[15] 3801T/C and 2455A/G were each individually associated with the risk of prostate cancer. Beer and colleagues[18] performed genotyping of *CYP1A1* (Ile/Val) gene in 117 patients with prostate cancer and 183 population-based controls. Their cohort failed to identify a relationship between the above polymorphisms and prostate cancer. Atkas and coworkers[19] studied the association of *CYP1A1* with prostate cancer in 100 patients and 107 controls of Turkish origin. No statistical differences were observed in the distribution of the *CYP1A1* Ile/Val genotype between the two groups (OR, 1.076; 95% CI, 0.605 to 1.913). However, the patients with *CYP1A1* Val/Val revealed a 2.8-fold higher risk of having prostate cancer than those with the wild-type Ile/Ile (OR, 2.846; 95% CI, 1.004 to 8.064).

Vijayalakshmi and associates[29] investigated the

association between two SNP's in South Indian population. Individuals with w1/m1 genotype at 3'UTR of *CYP1A1* were at a higher risk of prostate cancer (OR, 4.64; 95% CI, 1.51 to 14.86; $P < .01$), while the *CYP1A1* Ile/Val genotype (w2/m2) on exon 7 was found to be associated with a decreased risk of the cancer (OR, 0.17; 95% CI, 0.02 to 0.89; $P = .03$). Different grades of tumors did not have a significant association with the variant genotypes. The role of *CYP1A1*, cigarette smoking, and age was analyzed by Mittal and Srivastava[20] in 130 patients with prostate cancer and 140 controls using polymerase chain reaction assay and binary logistic regression model. The T/C polymorphism of *CYP1A1* revealed a significant association with smoking for prostate cancer risk. Li and colleagues[21] analyzed *CYP1A1* with respect to genetic susceptibility to prostate cancer in Chinese men. They genotyped 208 patients and 230 age-matched controls and analyzed the results according to age at diagnosis, prostate-specific antigen levels, and cancer stage and grade (Gleason score). No significant differences in the frequency distributions of *CYP1A1* polymorphisms were observed between the patients and the controls.

In another study, *CYP1A1* was analyzed in a case-control fashion, but the data was not statistically significant after appropriate corrections for multiple comparisons.[16] Yang and colleagues[22] investigated the association of cytochrome P450 1A1, smoking, alcohol drinking, and the risk of prostate cancer in a Han population in Southern China (225 patients and 250 age-matched controls). The *CYP1A1* Val/Val genotype significantly increased the risk of prostate cancer (OR, 2.26; 95% CI, 1.09 to 4.68). Heavy smoking history (OR, 1.61; 95% CI, 1.04 to 2.50) significantly increased the susceptibility of prostate cancer.

Nock and coworkers[17] investigated the relationship between cigarette smoking and *CYP1A1* Ile/Val polymorphism using a family-based case-control design (439 patients with prostate cancer and 479 controls); however, the results were not statistically significant. In another study, 83 patients and 115 age-matched healthy controls were genotyped for genetic polymorphisms of *CYP1A1* by the genechip technique. There were no significant differences in the frequency of *CYP1A1* polymorphisms between the patients and the healthy controls.[30] Silig and colleagues[23] studied on *CYP1A1*-MspI in 321 Turkish individuals (152 patients with prostate cancer and 169 age-matched controls). No association was observed between *CYP1A1* polymorphism and prostate cancer or smoking history. Associations between genetic polymorphisms of *CYP1A1* and prostate cancer were analyzed by Murata and associates[32] in a case-control study of 315 individuals. The frequency of Val/Val genotypes for *CYP1A1* was 11.3% in patients with cander compared with 5.5% in controls. This polymorphism, thus, was associated with a significantly increased risk of prostate cancer (OR, 2.4; 95% CI; 1.01 to 5.57). The study also confirmed that the *CYP1A1* polymorphism in combination with glutathione S-transferase M1 (*GSTM1*) gene polymorphism may be associated with prostate cancer susceptibility in the Japanese population.

Gao and colleagues[9] studied the possible relationship between *CYP1A1* genetic polymorphisms and the susceptibility of prostate cancer in 48 patients and 112 healthy individuals. Among patients and their matched controls, the frequencies of alleles and genotypes were significantly different with Ile/Val gene polymorphisms ($P < .05$); the allele G and GG genotypes were significantly more frequent than those in the controls with an (OR, 1.59 and OR, 3.06; respectively). But, no significant differences of the frequencies of the MspI alleles and genotypes were found between the patients with prostate cancer and the controls.

The association between genetic polymorphisms of *CYP1A1* and familial prostate cancer risk was examined in a case-control study of 185 individuals by Suzuki and associates.[24] The presence of any mutated alleles significantly increased cancer risk in comparison with wild-type genotypes by combination analysis (OR, 2.38; 95% CI, 1.72 to 3.29; $P = .007$). Acevedo and colleagues[25] studied on the associations between *CYP1A1* Msp1 and prostate cancer in a case-control study. Their findings suggest that the

Chilean carrying single or combined *GSTM1* and *CYP1A1* polymorphisms were more susceptible to prostate cancer. Caceres and colleagues[26] suggested that the interaction between genetic polymorphisms in *GST* (T1;M1) and *CYP1A1* M1 would play a significant role as a modifying factor on prostate cancer risk in Chilean people. Figer and coworkers[27] showed in 224 patients that *CYP1A1* gene polymorphisms did not show a significant association with prostate cancer. Finally, Murata and coworkers[28] analyzed genetic polymorphisms of the xenobiotic-metabolizing enzymes, *CYP1A1*, and *GSTM1* in 115 patients with cancer and 204 controls. The *CYP1A1* Val/Val genotype significantly increased the risk of prostate cancer (OR, 2.6; 95% CI, 1.11 to 6.25) and the Ile/Val genotype showed a similar tendency (OR, 1.4; 95% CI, 0.86 to 2.29). The combination of the *CYP1A1* Val allele and *GSTM1* (0/0) genotype was associated with a higher risk (OR, 2.3; 95% CI, 1.18 to 4.48) than the CYP1A1 Val allele alone.

CONCLUSION

This meta-analysis included data from 14 case-control comparisons with approximately 6000 genotyped patients with prostate cancer and controls. The overall data demonstrated that the *CYP1A1* G/A polymorphism is unlikely to be a major risk factor of prostate cancer on a wide population basis. However, although individual studies have shown conflicting results, the T/C polymorphism may considerably influence the risk of this cancer.

The *CYP1A1* polymorphism, therefore, may be an important population-wide risk factor of prostate cancer with respect to the T/C polymorphism. This meta-analysis could not address conclusively familial prostate cancer because hereditary forms of this cancer with many members affected in a family are not very common. Future studies are being planned to explore whether the *CYP1A1* polymorphism may have any effects on the risk of prostate cancer specifically in this setting. Control groups of the different studies were not well characterized as to the extent of inclusion of subjects with benign prostatic hyperplasia, which may again affect the results. Studies are also planned to determine the influence of T/C polymorphism with the risk of prostate cancer on a wider population basis.

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CONFLICT OF INTEREST

None declared.

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