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Catalase C-262T polymorphism and risk of prostate cancer: Evidence from meta-analysis

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ABSTRACT

Catalase is an important endogenous antioxidant enzyme that detoxifies hydrogen peroxide to oxygen and water, thus limiting the deleterious effects of reactive oxygen species. Several studies investigated the role of the Catalase (CAT) C-262T gene polymorphism on the risk of prostate cancer (PCa), but get conflicting results. We performed a meta-analysis based on five studies, to determine whether Catalase C-262T polymorphism contributes to the risk of prostate cancer using odds ratios (OR) with 95% confidence intervals (CI). On the whole, our evidence indicates that CAT C-262T polymorphism significantly increases PCa risk in the allele comparison model (OR = 1.094, 95% CI = 1.015–1.178, P = 0.018). In the stratified analysis by ethnicity, the same results are found among Caucasians (allele model, OR = 1.090, 95% CI = 1.009–1.177, P = 0.028, dominant model, OR = 1.108, 95% CI = 1.023–1.201, P = 0.012, recessive model, OR = 1.379, 95% CI = 1.158–1.641, P = 0.000, homozygous model, OR = 1.429, 95% CI = 1.196–1.707, P = 0.000, and heterozygote model, OR = 1.224, 95% CI = 1.020–1.469, P = 0.030). In conclusion, this meta-analysis suggests a positive correlation between Catalase C-262T polymorphism and the development of PCa.

1. Introduction

There has been a progressive increase in the global incidence of prostate cancer (PCa) in the last two decades. The combination of genetic and environmental factors may explain the ethnic and geographical variations in the incidence and mortality from prostate cancer (Plata Bello and Concepcion Masip, 2014). Many studies generated considerable evidence of an inherited component to prostate cancer, genome-wide association studies (GWAS) have identified 76 susceptibility loci associated with prostate cancer risk (Eeles et al., 2014). Of these, much association between polymorphisms in prooxidant or antioxidant genes and prostate cancer risk was found, such as myeloperoxidase (MPO), superoxide dismutase (SOD2), and catalase (CAT) etc. (Geybels et al., 2014). Catalase is an important endogenous antioxidant enzyme that detoxifies hydrogen peroxide to oxygen and water, thus limiting the deleterious effects of reactive oxygen species (ROS) (Goyal and Basak, 2010). Therefore, the CAT plays an important role in substance metabolism, the polymorphism of CAT gene was associated with the development of diseases, for instance, systemic lupus erythematosus (Warchol et al., 2008), chronic obstructive pulmonary disease (Taniguchi et al., 2014), invasive cervical cancer (Castaldo et al., 2014), and prostate cancer (Karunasinghe et al., 2012; Tefik et al., 2013).

The CAT gene is located on chromosome 11p13 and consists of 12 introns and 13 exons. There are different polymorphism sites in the CAT gene. Of which the variant T allele of the CAT C-262T gene polymorphism has been associated with lower enzyme activity compared with the C allele, and thus, increased levels of ROS (Ahn et al., 2006). Thus this kind of polymorphism was widely studied and considered to be associated with risk of prostate cancer. Three studies proposed that CAT C-262T gene polymorphism may have a significant influence on the development of PCa (Karunasinghe et al., 2012; Tefik et al., 2013; Geybels et al., 2014), whereas two other studies could not confirm this association (Choi et al., 2007; Ding et al., 2012). In order to investigate the association between CAT C-262T polymorphism and the risk of PCa, we conducted this meta-analysis.

2. Materials and methods

2.1. Publication search strategy

A comprehensive and systematic search through the PubMed and Embase databases was performed using these terms as follows: "CAT" or "catalase", "polymorphism" or "gene mutation" or "gene variation", "prostate cancer" or "prostate neoplasm" (the last search was updated October 20, 2014). There were no language and sample size limitation

Abbreviations: CAT, catalase; PCa, prostate cancer; OR, odds ratios; CI, confidence intervals; GWAS, genome-wide association studies; MPO, myeloperoxidase; SOD2, superoxide dismutase; ROS, reactive oxygen species

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in the included studies. All relevant publications were reviewed. Articles in reference lists were also hand-searched for potentially relevant publications. When more than one of the same or overlapping populations were included in several studies, only the most recent or complete study was used for this meta-analysis.

2.2. Inclusion and exclusion criteria

Studies included in this meta-analysis should meet the following criteria: (1) case–control studies or cohort studies; (2) evaluation of CAT C-262T polymorphism and PCa risk; and (3) sufficient data for examining an odds ratio (OR) with 95% confidence interval (95% CI). Major reasons for exclusion of studies were as follows: (1) not for PCa research; (2) only case population acquired without additional data; (3) duplicate publication; and (4) the distribution of genotypes among controls is not in Hardy–Weinberg equilibrium.

2.3. Data extraction

The eligible data were extracted by two investigators (Hu and Feng), and consensus was reached by discussion. Some important information was extracted from each study: first author's name, year of publication, ethnicity, sample size of cases and controls, numbers of cases and controls with the CC, CT, TT genotypes, and genotyping methods. The different ethnic populations were classified in African, Asian and Caucasian.

2.4. Statistical analysis

OR with 95% CI was used to measure the strength of association of the CAT C-262T polymorphism with prostate cancer risk. The statistical significance of the pooled OR was assessed using a Z test with a two-tailed $P < 0.05$ considered to be statistically significant. Hardy–Weinberg equilibrium in the control group was tested using the Pearson chi-square test for goodness of fit, $P < 0.05$ was considered significant. We evaluated the risk using the homozygote model (CC vs. TT), heterozygote model (CT vs. TT), dominant model [(TT+CT) vs. CC], recessive model [TT vs. (CT+CC)], and allele comparison model (C-allele vs. T-allele). We also carried out the stratified analysis by ethnicity. Statistical heterogeneity among studies was evaluated using I^2 statistics (ranges from 0 to 100%), λ^2 test, and P values (Zintzaras and Ioannidis, 2005). The fixed effects model method (Mantel–Haenszel) was used, except when a significant Q test ($P < 0.05$) or $I^2 > 50\%$ indicated the existence of heterogeneity among studies, when it was indicated the existence of heterogeneity, the random effects model (DerSimonian–Laird method) was applied (Sacks et al., 1987). Heterogeneity was also explored in subgroup analysis with ethnic groups (African, Asian, and Caucasian). Sensitivity analysis was performed to assess the stability of results. Funnel plots were drawn to estimate the potential publication bias, in which the standard error of log (OR) of each study was plotted against its log (OR). Whether the funnel plot was symmetry or not was assessed with Egger's test (Egger et al., 1997). When using Egger's test to assess the publication bias, $P < 0.05$ was considered statistically significant. All statistical tests for this meta-analysis were performed with STATA 12.0.

3. Results

3.1. Characteristics of included studies

A total of 19 potentially relevant papers were identified based on the search strategy. Five studies with 3865 cases and 28,224 controls were finally included into this meta-analysis (Choi et al., 2007; Ding et al., 2012; Karunasinghe et al., 2012; Tefik et al., 2013; Geybels et al., 2014). The characteristics of the included studies were listed in Table 1. Of these five studies, three studied the Caucasian population (Karunasinghe et al., 2012; Tefik et al., 2013; Geybels et al., 2014), and one studied the Caucasian and African American population as a mixed study; we extracted the Caucasian and African American population separately (Choi et al., 2007), and noticed that there was a small population that did not know distinct ethnicity in this mixed study. Another one studied the Asian population (Ding et al., 2012). The patients with PCa were confirmed histologically or pathologically in most studies. Genotyping methods were all polymerase chain reaction–restriction fragment length polymorphism except one (Ding et al., 2012) genotyped by MassARRAY iPLEX.

3.2. Quantitative synthesis

The association between CAT C-262T polymorphism and PCa risk was investigated in five studies of which three were in Caucasian population, one in Asian population, one in Caucasian and African population. The CAT genotypes CC, CT, and TT were observed in 70.4, 25.0, and 4.6% of the prostate cancer patients and in 63.7, 31.4, and 4.9% of controls. The pooled data indicated significant association between CAT C-262T polymorphism and risk of PCa; several models were calculated, including allele comparison model (OR = 1.094, 95% CI = 1.015–1.128, $P_{heterogeneity} = 0.770$, P = 0.018, Fig. 1), dominant model (OR = 1.113, 95% CI = 1.030–1.202, $P_{heterogeneity} = 0.653$, P = 0.007, data not shown), recessive model (OR = 1.389, 95% CI = 1.168–1.653, $P_{heterogeneity} = 0.692$, P = 0.000, data not shown), homozygous model (OR = 1.446, 95% CI = 1.212–1.725, $P_{heterogeneity} = 0.597$, P = 0.000, data not shown), and heterozygote model (OR = 1.226, 95% CI = 1.023–1.470, $P_{heterogeneity} = 0.947$, P = 0.028, data not shown). Subgroup analyses were carried out according to the ethnicity, one study (Choi et al., 2007) was mixed population, as a combination of the Caucasian and African studies. We separated it into two subgroups. In the stratified analysis by ethnicity, significantly increased risks were found among Caucasians (allele model, OR = 1.090, 95% CI = 1.009–1.177, $P_{heterogeneity} = 0.491$, P = 0.028, Fig. 2; dominant model, OR = 1.108, 95% CI = 1.023–1.201, $P_{heterogeneity} = 0.332$, P = 0.012, Fig. 3; recessive model, OR = 1.379, 95% CI = 1.158–1.641, $P_{heterogeneity} = 0.483$, P = 0.000, homozygous model, OR = 1.429, 95% CI = 1.196–1.707, $P_{heterogeneity} = 0.356$, P = 0.000, and heterozygote model, OR = 1.224, 95% CI = 1.020–1.469, $P_{heterogeneity} = 0.866$, P = 0.030, Fig. 3S). The association of C-262T polymorphism and PCa risk in the African population needs more data to calculate; the association in the Asian population is not statistically significant.

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

First author (reference)	Year	Ethnicity	Sample size		Cases			Controls		
			Case	Control	CC	CT	TT	CC	CT	TT
Guanxiong Ding	2012	Asian	1417	1008	1316	99	2	940	67	1
Milan S. Geybels	2014	Caucasian	1527	25,184	887	539	103	15,794	8108	1282
Ji-Yeob choi	2007	Mixed	508	1403	317	165	26	885	461	57
Tzevat Tefik	2013	Caucasian	155	195	58	64	33	107	68	20
Nishi Karunasinghe	2012	Caucasian	258	434	144	99	15	258	160	16