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Meta-Analysis

Matrix metalloproteinase-1 (MMP-1) rs1799750 polymorphism is associated with nasopharyngeal carcinoma (NPC) risk

L. Cao*, P. Li, L. Dong

E.N.T. Department, The Affiliated Hospital to Changchun University of Chinese Medicine, Changchun 130021, Jilin, China

Correspondence to: jinggu46doulian1@163.com

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Abstract: A few studies suggested that matrix metalloproteinase 1 (MMP-1) rs1799750 polymorphism was associated with nasopharyngeal carcinoma (NPC) risk. However, other studies did not confirm this result. Thus, we did this meta-analysis to evaluate the association between MMP-1 rs1799750 polymorphism and NPC risk. We searched PubMed and EMBASE. Five studies with 1497 cases and 1643 controls were included in this meta-analysis. Subjects with MMP-1 rs1799750 polymorphism had an decreased NPC risk (OR = 0.79; 95%CI, 0.69–0.91; P = 0.0007; I^2 = 70%). In the subgroup analysis by smoking, a marginally significant association was found in non-smokers (OR = 0.73, 95% CI 0.52 – 1.04, *P* = 0.08; I^2 = 0%) but not smokers (OR = 0.59, 95% CI 0.24 – 1.42, *P* = 0.24; I^2 = 83%). In conclusion, this meta-analysis showed that MMP-1 rs1799750 polymorphism was significantly associated with NPC risk.

Key words: Nasopharyngeal carcinoma; Matrix metalloproteinase; Genetic.

Introduction

Nasopharyngeal carcinoma (NPC) is a malignant head and neck cancer, which has a relatively high incidence of 20-30 per 100000 in endemic areas such as southern China and Southeast Asia (1). NPC is one of the most frequent virus-related malignancies in humans. Epstein-Barr virus (EBV) plays an important role in the NPC development (2). However, EBV is not the unique etiological factor of NPC, genetic factors also play a role in the development of NPC (3)

Matrix metalloproteinases (MMPs) are zinc- and calcium-dependent endoproteinases that have the ability to break down extracellular matrix (4). MMP-1 has been the subject of a broad range of experimental studies and important conclusions have been drawn about the conformational behavior of MMP-1 domains in solution. A few studies suggested that MMP-1 rs1799750 polymorphism was associated with NPC risk. However, other studies did not confirm this result (5-9). Thus, we did this meta-analysis to evaluate the association between MMP-1 rs1799750 polymorphism and NPC risk.

Materials and Methods

Search for publications

We searched PubMed and EMBASE with the following words: “Nasopharyngeal carcinoma”, “Nasopharyngeal tumor”, “Matrix metalloproteinase-1” and “MMP1”. We did not restrict publication language and time. The references of the eligible studies were also searched.

Inclusion and exclusion criteria

The inclusion criteria were: (1) case–control studies; (2) investigatws the association between MMP-1 rs1799750 polymorphism and NPC risk; (3) reported odds ratios (ORs) with 95% confidence intervals (CIs). The major criteria for exclusion of studies were: (1) reviews and repeated literatures; (2) case-only studies; (3) studies without reporting Ors and 95% CIs.

Data extraction

Two authors extracted the data independently. These data included: the first author, year, country, race, age, gender, and sample size.

Statistical analysis

A statistical test for heterogeneity was performed based on the Q statistic. The *P*>0.10 of the Q-test indicated a lack of heterogeneity among studies. The random-effects model was used to estimate the pooled OR. A Chi square-test was used to determine if observed frequency of genotype in control population conformed to Hardy-Weinberg equilibrium (HWE) expectations. Subgroup analysis was conducted by the smoking status. Sensitivity analysis and Galbraith plots were performed. All statistical tests were performed with Revman 5.1 software (Nordic Cochrane Center, Copenhagen, Denmark) and Stata software 11.0 (Stata Corporation, College Station, TX). A *P* value <0.05 was considered statistically significant.

Results

Characteristics of the included studies

Finally, five studies were included in this meta-

Table 1. Characteristics of the included studies.

First author	Year	Country	Ethnicity	Age	Gender	Number of case (n)	Number of control (n)	Hardy-Weinberg equilibrium
Kondo 1	2005	Japan	Asian	Adult	Mixed	44	59	Yes
Kondo 2	2005	Japan	Asian	Adult	Mixed	39	23	Yes
Zhou 1	2007	China	Asian	Adult	Mixed	593	480	Yes
Zhou 2	2007	China	Asian	Adult	Mixed	239	286	Yes
Nasr	2007	Tunisia	African	Adult	Mixed	174	171	Yes
Gao	2010	China	Asian	Adult	Mixed	232	272	Yes
Tsai	2016	China	Asian	Adult	Mixed	176	352	Yes

analysis. A total of 1497 cases and 1643 controls were included. All studies used Asian populations, however, only one study used African population. All included subjects were adults. The characteristics of each study included in this meta-analysis are presented in Table 1.

Quantitative data synthesis

As shown in Figure 1, subjects with MMP-1 rs1799750 polymorphism had an decreased NPC risk (OR = 0.79; 95%CI, 0.69–0.91; P = 0.0007; I^2 = 70%). In the subgroup analysis by smoking, a marginally significant association was found in non-smokers (OR = 0.73, 95% CI 0.52 – 1.04, P = 0.08; I^2 = 0%) but not smokers (OR = 0.59, 95% CI 0.24 – 1.42, P = 0.24; I^2 = 83%; Figure 2).

Sensitivity analysis was performed through sequentially omitted individual studies. None of the results were materially changed, which suggested the robustness of our results (Figure 3). There was significant heterogeneity in the meta-analysis (I^2 = 70%). The Galbraith plot was conducted. As shown in Figure 4, 2 studies were the outliers. After excluding these 2 studies, the heterogeneity decreased and there was no obvious heterogeneity (I^2 = 23%). The result was still statistically significant (OR = 0.79, 95% CI 0.69 – 0.90, P = 0.0006). The shape of the funnel plot was symmetrical (Figure 5). Egger's test indicated no significant publication bias (P = 0.13).

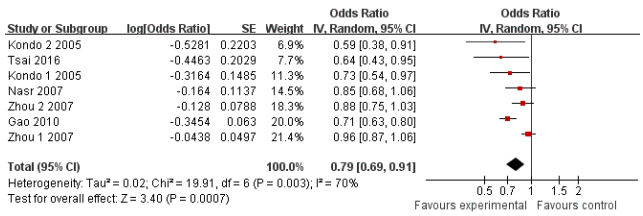

Figure 1. The association between MMP-1 rs1799750 polymorphism and NPC risk.

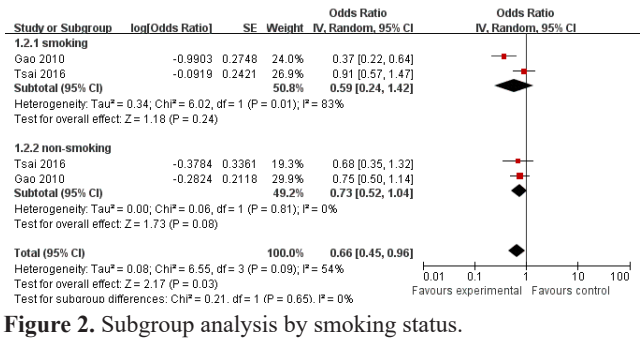

Figure 2. Subgroup analysis by smoking status.

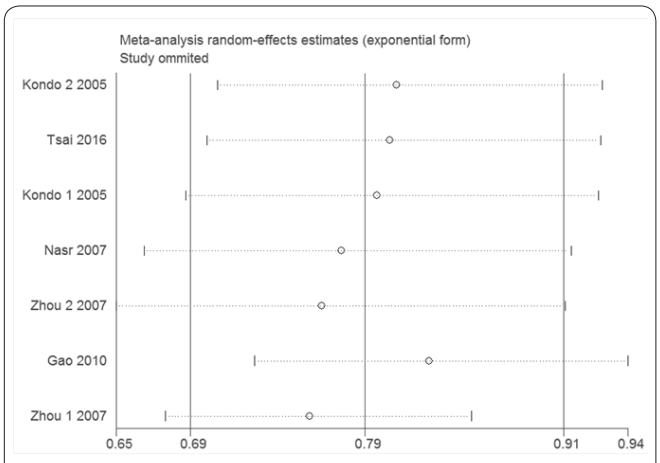

Figure 3. Sensitivity analysis of the association between MMP-1 rs1799750 polymorphism and NPC risk.

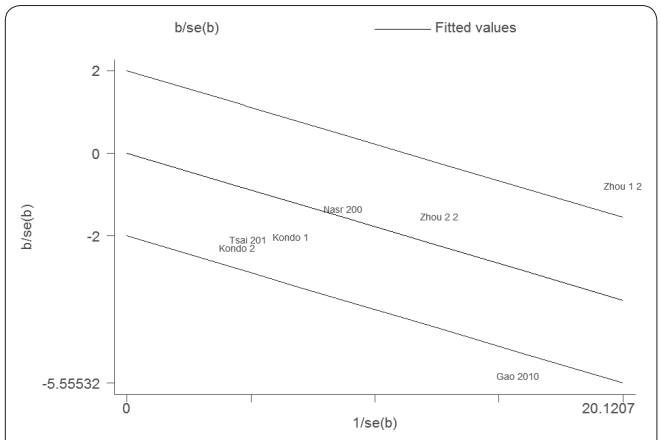

Figure 4. Galbraith plot of the association between MMP-1 rs1799750 polymorphism and NPC risk.

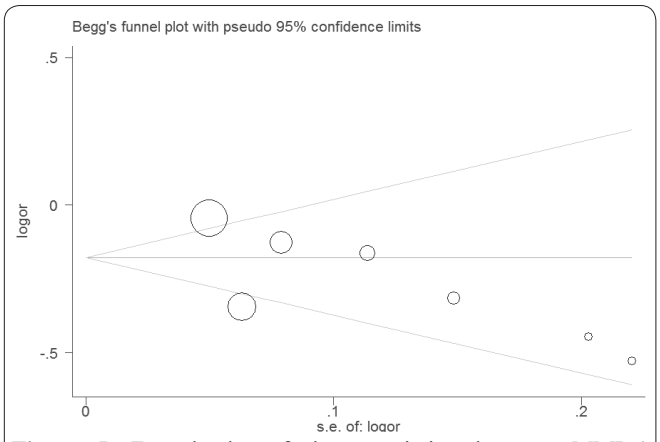

Figure 5. Funnel plot of the association between MMP-1 rs1799750 polymorphism and NPC risk.

Discussion

Lu et al. suggested that polymorphism MMP1 -1607 1G>2G is significantly associated with a significantly increased risk of cancers (10). Zhang et al. suggested that the MMP1 -1607 1G>2G polymorphism is associated with risk of head and neck cancer (11). Xiao et al. showed a significant association between MMP1-1607 1G/2G polymorphism and lung cancer risk (12). In this meta-analysis, we found that subjects with MMP-1 rs1799750 polymorphism had an decreased NPC risk. In the subgroup analysis by smoking, a marginally significant association was found in non-smokers but not smokers.

Nasr et al. found that MMP-1 rs1799750 polymorphism was associated with the aggressive forms of NPC as defined by large tumor size (T3-T4), lymph node metastasis and advanced stages (III-IV) at the time of diagnosis (5). Furthermore, they showed a significant association between MMP-1 rs1799750 polymorphism with reduced disease-free survival for NPC patients (5). This result was confirmed by other study (8). Thus, MMP-1 rs1799750 polymorphism had independent prognostic significance for NPC.

Our meta-analysis had some limitations. First, the numbers of published studies were not sufficient for a comprehensive analysis, particularly for Africans. Second, significant heterogeneity was found in this meta-analysis. However, heterogeneity did not seem to influence the result. Third, the sample size was small, and thus the power of the study was not sufficient. Fourth, we did not confirm if the result was still positive in genome-wide association studies. Last, we did not perform the Bonferroni correction in this study.

In conclusion, this meta-analysis showed that MMP-1 rs1799750 polymorphism was significantly associated with NPC risk.

Disclosure of conflict of interest

The authors have declared that no competing interests exist.

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