Meta-Analysis

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

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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; I² = 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; I² = 0%) but not smokers (OR = 0.59, 95% CI 0.24 – 1.42, P = 0.24; I² = 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.
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; I² = 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; I² = 0%) but not smokers (OR = 0.59, 95% CI 0.24 – 1.42, P = 0.24; I² = 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 (I² = 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 (I² = 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).

**Table 1.** Characteristics of the included studies.

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Country</th>
<th>Ethnicity</th>
<th>Age</th>
<th>Gender</th>
<th>Number of case (n)</th>
<th>Number of control (n)</th>
<th>Hardy-Weinberg equilibrium</th>
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<tr>
<td>Kondo 1</td>
<td>2005</td>
<td>Japan</td>
<td>Asian</td>
<td>Adult</td>
<td>Mixed</td>
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<td>59</td>
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<tr>
<td>Kondo 2</td>
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<td>Japan</td>
<td>Asian</td>
<td>Adult</td>
<td>Mixed</td>
<td>39</td>
<td>23</td>
<td>Yes</td>
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<tr>
<td>Zhou 1</td>
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<td>China</td>
<td>Asian</td>
<td>Adult</td>
<td>Mixed</td>
<td>593</td>
<td>480</td>
<td>Yes</td>
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<tr>
<td>Zhou 2</td>
<td>2007</td>
<td>China</td>
<td>Asian</td>
<td>Adult</td>
<td>Mixed</td>
<td>239</td>
<td>286</td>
<td>Yes</td>
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<tr>
<td>Nasr</td>
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<td>Tunisia</td>
<td>African</td>
<td>Adult</td>
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<tr>
<td>Gao</td>
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<td>Adult</td>
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<td>272</td>
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<tr>
<td>Tsai</td>
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<td>China</td>
<td>Asian</td>
<td>Adult</td>
<td>Mixed</td>
<td>176</td>
<td>352</td>
<td>Yes</td>
</tr>
</tbody>
</table>
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.

References