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The association between MMP2, MMP3, and MMP9 promoter polymorphisms and head and neck cancer risk

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He, PF[1]; Li, WH[2]; Lian, Y[3].

Corresponding author:
Pengfei He

hpf89@qq.com

Author Affiliation:
Sichuan Stomatological Hospital, Chengdu, China.

ADMINISTRATIVE INFORMATION

Support - Chengdu Health and Health Commission (No. 2019026).

Review Stage at time of this submission - Piloting of the study selection process.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202410018

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 January 2024 and was last updated on 06 January 2024.

INTRODUCTION

Review question / Objective The relationship between MMP2, MMP3, and MMP9 promoter polymorphisms and head and risk of neck cancer (HNC) has been extensively studied, but the results were inconsistent. To get a more precise evaluation the association, we performed the meta-analysis.

Rationale Head and neck cancer (HNC) is the seventh-leading cancer worldwide and is a term that includes mucous carcinoma that arise in several locations, such as the oral cavity, paranasal, nasal cavity, larynx, pharynx and sinuses. It accounts for about 3% of all malignancies in the United States with 54,540 new cases and 11,580 deaths from HNC between 2005 and 2020. The important role of matrix metalloproteinases (MMPs) in HNC development has been established. There are three important members in MMP family: MMP2, MMP3, and MMP9. MMP2, MMP3, and MMP9 were found to be associated with several types of cancer risk, including HNC. There are several important single nucleotide polymorphisms (SNPs) in human MMP2, MMP3, and MMP9 promoter. MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms were related to the risk of various types of HNC, such as oral cancer, nasopharyngeal cancer, laryngeal squamous cell carcinoma.Although some researchers have observed the possible association between MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms and risk of HNC, their conclusions were different and even contradictory. Thus, we carried out a meta-analysis that included the latest data to investigate in particular the association between MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms and HNC risk.

Condition being studied Participants in this study have rich experience in systematic review and meta-analysis, especially in the study on the relationship between gene polymorphism and tumor, and 3 relevant studies have been published. The organization has sufficient database, software and hardware support. We were able to carry out this study completely and smoothly.

METHODS

Search strategy We use Newcastle-Ottawa Scale (NOS) to rate the caliber of the included studies. The study quality is classified as low, medium, or high based on scores of 0–3, 4–6, and 7–9, respectively. With the term“(MMP or (matrix metalloproteinase) or collagenase or gelatinase or matrilysin or PUMP) and ("oral cancer" or "oral carcinoma" or "oral squamous cell carcinoma" or "OSCC" or "oral SCC" or "head and neck cancer" or "head and neck carcinoma" or "HNSCC" or "salivary gland cancer" or "salivary gland tumor" or "laryngeal cancer" or "larynx cancer" or "nasopharyngeal cancer" or "nasopharyngeal carcinoma" or "hypopharyngeal cancer" or "pharyngeal cancer" or "hypopharynx squamous cell carcinoma" or "hypopharynx SCC" "oropharyngeal cancer" or "oropharyngeal carcinoma" or "pharynx cancer" or "larynx squamous cell carcinoma" or "larynx SCC") and ("variant" or "polymorphism" or "genotype" or "gene" or "allele")”, in the PubMed, EMBASE, Web of Science and China National Knowledge Infrastructure (CNKI) databases. All the publications until Dec. 31 2023.

Participant or population This study was based on a case-control study to explore the relationship between MMP and head and neck tumors. Selection criteria were (1) study the MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms and HNC risk; (2) case-control studies on irrelevant individuals; (3) reporting the genotype distributions of cases and controls and the odds ratio (OR) with 95% confidence interval (95%CI) could be calculated. If more than one published study using the same patient group, only the largest or the latest study would be used in this meta-analysis.

Intervention The MMP2, 3 and 9 polymorphisms genotypes of HNC patients.

Comparator Totally four polymorphisms are included in our analyze.

Study designs to be included case-control studies.

Eligibility criteria (1) study the MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms and HNC risk; (2) case-control studies on irrelevant individuals; (3) reporting the genotype distributions of cases and controls and the odds ratio (OR) with 95% confidence interval (95%CI) could be calculated. If more than one published study using the same patient group, only the largest or the latest study would be used in this meta-analysis.

Information sources PubMed, EMBASE, Web of Science and China National Knowledge Infrastructure (CNKI)databases.

Main outcome(s) The study will figure out the relationship between the MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms and HNC risk. We also conducte stratification analyses of cancer type and ethnicity.

Additional outcome(s) Non.

Data management The data, including first author, publication year, ethnicity, original country, gender, cancer site and source of control (population-based or hospital-based) were independently extracted by two members and reach a consensus on all data through consultation.

Quality assessment / Risk of bias analysis We use Newcastle-Ottawa Scale (NOS) to rate the caliber of the included studies. The study quality is classified as low, medium, or high based on scores of 0–3, 4–6, and 7–9, respectively.

Strategy of data synthesis We use crude odds ratios (ORs) and 95% confidence intervals (95% CIs) to evaluate the strength of the relationship between the MMP2-735 C>T, MMP2-1306 C>T, MMP3-1171 5A>6A and MMP9-1562 C>T polymorphisms and HNC risk and is determined by Z-test. The pooled ORs are performed for four genetic models including homozygote comparison, heterozygote comparison, recessive model and dominant model. The statistical significance of ORs is analyzed by Z test and $P < 0.05$ were taken as statistical significance. We also conduct stratification analyses of cancer type and ethnicity.

Subgroup analysis We conduct stratification analyses of cancer type (Nasopharynx, oral cavity, mixed HNC), ethnicity(Asian, Caucasian, African) and source of control(public based and hospital based).

Sensitivity analysis Heterogeneity is analyzed by Q-test and I2 value ranging from 0% to 100% to describe the percentage of between-study variation caused by heterogeneity. P value for the Q-test less than 0.10 indicates heterogeneity among studies. When P heterogeneity is less than 0.10, a random-effect model is applied; If not, a fixed-effect model is applied. Galbraith plot will be used to detect the potential sources of heterogeneity. To analyze the stability of the results, a sensitivity analysis is performed. Begg's funnel plot is used to analyze the publication bias and Egger's test is used to measure the degree of asymmetry. All of the statistical analyses are performed by the software STATA11.0.

Language restriction English and Chinese.

Country(ies) involved China.

Other relevant information Non

Keywords head and neck cancer, MMP, polymorphism, systematic review.

Dissemination plans We will write a manuscript and submit to related journal.

Contributions of each author

Author 1 - Pengfei He - (I) Conception and design; (II) Administrative support; (III) Provision of study materials or patients; (IV) Collection and assembly of data; (V) Data analysis and interpretation; (VI) Manuscript writing; (VII) Final approval of manuscript.
Email: hpf89@qq.com
Author 2 - Wenhui Li - (I) Conception and design; (II) Administrative supporti; (III) Provision of study materials or patients; (IV) Collection and assembly of data; (V) Data analysis and interpretation;(VI) Manuscript writing; (VII) Final approval of manuscript.
Email: 693170665@qq.com
Author 3 - Lian Yang - (III) Provision of study materials or patients; (IV) Collection and assembly of data; (V) Data analysis and interpretation;(VI) Manuscript writing; (VII) Final approval of manuscript.
Email: 946019981@qq.com