

SUSCEPTIBILITY OF MMP3 GENE POLYMORPHISM TO CORONARY ARTERY DISEASE: A META-ANALYSIS

OSETLJIVOST POLIMORFIZMA GENA MMP3 NA BOLEST KORONARNIH ARTERIJA: META-ANALIZA

Wenwang Liu

Department of Clinical Laboratory, Beijing Hospital of Integrated Chinese & Western Medicine, Beijing China

Summary

Background: Conclusions on susceptibility of MMP3 -1612 5A/6A to morbid risk of coronary artery disease (CAD) are controversial. This meta-analysis aims to obtain the accurate relationship between them.

Methods: Relevant literatures on susceptibility of MMP3 -1612 5A/6A to morbid risk of CAD published before July 2019 were searched in PubMed, Web of Science, Cochrane Library, CNKI, VIP and Wanfang. Data were extracted from eligible literatures and analyzed by RevMan5.3 and STATA12.0 for calculating OR and corresponding 95% CI. Study selection: A total of 18 literatures reporting MMP3-1612 5A/6A and CAD were enrolled. Data extraction was conducted by two researches independently. Any disagreement was solved by the third research.

Results: In recessive model (OR=1.3, 95% CI=1.2–1.64, P=0.03) and over-dominant model (OR=1.50, 95% CI=1.14–1.97, P=0.002), MMP3 -1612 5A/6A was correlated to susceptibility of CAD. Subgroup analysis uncovered that in different genetic models, MMP3 -1612 5A/6A was correlated to susceptibility of CAD in East Asian population (mainly Chinese population).

Conclusion: MMP3 -1612 5A/6A is closely linked to morbid risk of CAD. Gene-environment interaction is the research focus in future analyses.

Keywords: MMP3, CAD, polymorphism

Kratak sadržaj

Uvod: Zaključci o podložnosti MMP3 -1612 5A/6A morbidnom riziku od koronarne arterijske bolesti (CAD) su kontroverzni. Ova meta-analiza ima za cilj da dobije tačan odnos između njih.

Metode: Relevantna literatura o podložnosti MMP3 -1612 5A/6A morbidnom riziku od CAD objavljena pre jula 2019. pretražena je u PubMed-u, Web of Science, Cochrane Library, CNKI, VIP i Wanfang. Podaci su izvučeni iz kvalifikovane literature i analizirani od strane RevMan5.3 i STATA12.0 za izračunavanje OR i odgovarajući 95% CI. Izbor studije: Ukupno 18 literatura koja izveštava o MMP3-1612 5A/6A i CAD je upisano. Ekstrakciju podataka sprovela su dva istraživanja nezavisno. Bilo kakvo neslaganje je rešeno trećim istraživanjem.

Rezultati: U recesivnom modelu (OR=1,3, 95% CI=1,2–1,64, P=0,03) i naddominantnom modelu (OR=1,50, 95% CI=1,14–1,97, P=0,002), MMP3 -1612 5A/6A je u korelaciji sa osetljivošću na CAD. Analiza podgrupe je otkrila da je u različitim genetskim modelima, MMP3 -1612 5A/6A bio u korelaciji sa osetljivošću na CAD u populaciji istočne Azije (uglavnom u kineskoj populaciji).

Zaključak: MMP3 -1612 5A/6A je usko povezan sa morbidnim rizikom od CAD. Interakcija gen-sredina je fokus istraživanja u budućim analizama.

Cljučne reči: MMP3, CAD, polimorfizam

Address for correspondence:

Wenwang Liu, MM.
Department of Clinical Laboratory,
Beijing Hospital of Integrated Chinese & Western
Medicine, 3 East Yongding Road, Haidian District,
Beijing 100039, China
Tel: 86013691210780
e-mail: lww16032810@163.com

Introduction

Coronary artery disease (CAD) is a heart disease caused by stenosis or obstruction of the coronary artery lumen due to coronary atherosclerosis, as well as functional changes that lead to myocardial ischemia, hypoxia, or necrosis. CAD is also referred to as ischemic heart disease, and it is the most common subtype of atherosclerosis-related lesions that significantly impact human health (1). CAD primarily affects individuals over 40 years of age, and it is more prevalent in men than in women. In recent years, the incidence of CAD has markedly increased in our country (1).

The matrix metalloproteinase (MMP) family consists of more than 20 secretases or ectocellular enzymes that degrade extracellular matrix proteins, coagulation factors, lipoproteins, latent growth factors, chemokines, and cell adhesion molecules (2, 3). Dysregulated extracellular matrix (ECM) metabolism is of significance in vascular remodeling during the progression and complication period of atherosclerosis (4). MMP3 not only degrades ECM components, but also activates MMP1 and other family members (5). With the advanced progression achieved on DNA technologies, MMP3 gene polymorphisms in the promoter region have been identified. In particular, MMP3 5A/6A is closely related to multiple pathological states (6). Therefore, we speculated that MMP3 gene polymorphisms may be related to susceptibility of CAD.

Numerous studies have evaluated the involvement of MMP3 gene polymorphisms in CAD; however, the results have often been non-replicable (7-9). This may be attributed to racial-specific genetic characteristics, insufficient sample sizes, improper selection of patients and controls, and a lack of adjustments for confounding factors. In this study, we extracted data from eligible literature to assess the involvement of MMP3 -1612 5A/6A in the susceptibility of CAD. Additionally, we explored the heterogeneity among enrolled literature and the existence of publication bias.

Materials and Methods

The meta-analysis of observational research poses a particular challenge due to the inherent biases and differences in research design. Therefore, we performed this analysis in accordance to the guiding principles of the meta-analysis of observational studies in epidemiological statements (10).

Searching strategy

Relevant literatures on susceptibility of MMP3 -1612 5A/6A to morbid risk of CAD published before July 2019 were searched in PubMed, Web of Science,

Cochrane Library, CNKI, VIP and Wanfang. Key words were searched as follows: MMP3, coronary heart disease/coronary syndrome/myocardial infarction/atherosclerosis and gene/allele/genotype/polymorphism/variation.

Study selection

Eligible full-text literatures were searched after reviewing titles and abstracts. Citations were manually searched. Data were extracted from recent or most complete publications. When an article contained more than one homogenous features (i.e. the end-points of CAD and MI), each feature was separately analyzed.

Inclusion/exclusion criteria

Inclusion criteria included: 1) Independent case-control studies analyzing hospital-based or population-based subjects without any language limitations. 2) Data were complete to obtain or calculate genotype frequencies. 3) Literatures reporting susceptibility of MMP3 -1612 5A/6A to morbid risk of CAD. 4) Genotype distribution in the controls was in accordance to HWE (Hardy-Weinberg equilibrium). 5) None of repeated published data.

Exclusion criteria: 1) Reviews, comments, animal experiments, mechanism researches and case reports. 2) Repeatedly published articles. 3) Studies with inadequate data.

Flow diagram of the publication selection was depicted in *Figure 1*.

Data extraction

Data were independently extracted and analyzed by two researchers. Any disagreement was solved by the third researcher. The following data were extracted from each literature: 1) Baseline characteristics of enrolled literature, including published magazine, first author, publish time, etc. 2) Baseline characteristics of subjects, including case number, country of publication, genotype number and distribution, HWE, etc.

Statistical analysis

Published data were synthesized when three or more studies reporting the same gene polymorphism. Once genotype data were provided, χ^2 test was applied in the control group.

Heterogeneity test was conducted by calculating OR and the corresponding 95% CI with the I^2 test and the Q test. The pooled OR in studies lacking the heterogeneity was calculated by the fix-effects model;

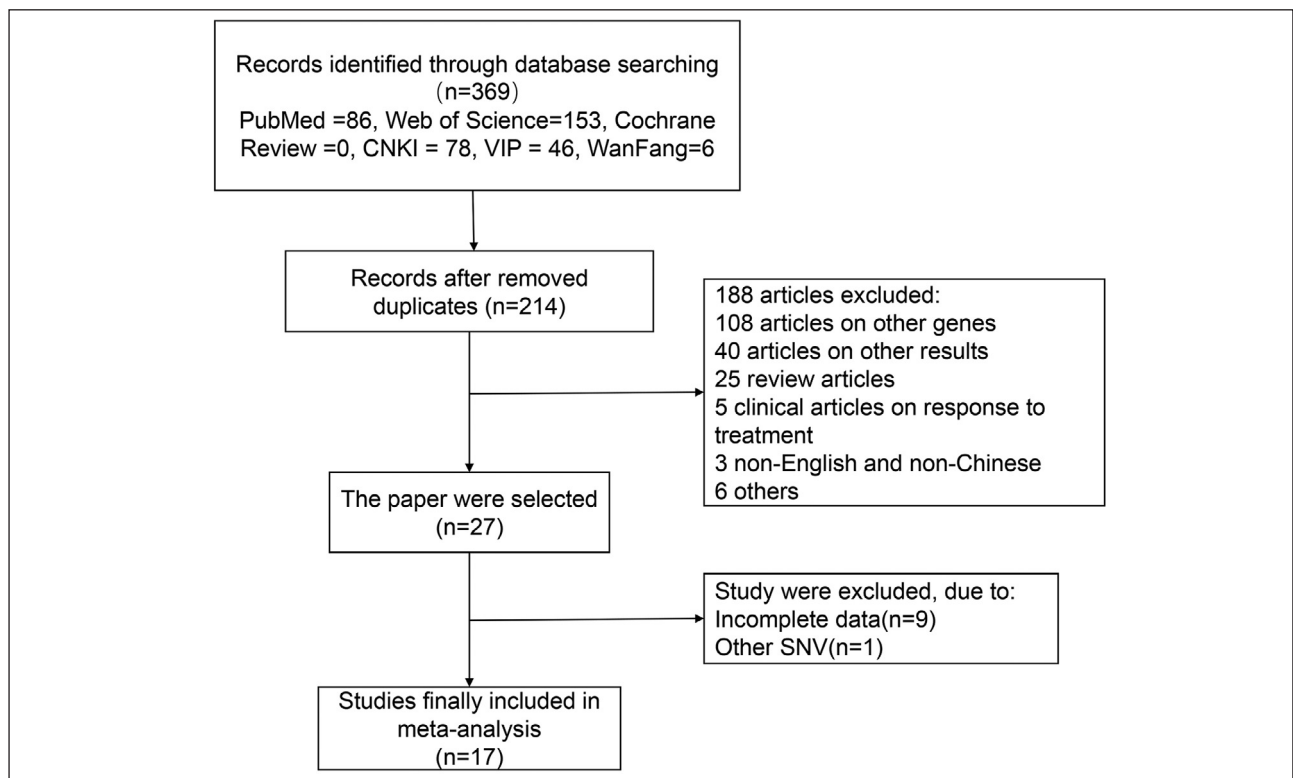


Figure 1 Flow diagram of the publication selection process.

otherwise, a random-effects model was used. Publication bias was evaluated by depicting funnel plots and quantified by Egger's test. Data analyses were conducted using RevMan 5.3 and STATA12.0 (London, UK).

Results

Baseline characteristics of enrolled literatures

Initially, a total of 369 literatures were searched and 155 replicates were excluded. After reviewing titles and abstracts, 188 irrelevant literatures (108 literatures reporting other genes, 40 reporting other endpoints, 25 reviews, 5 case reports, 3 published in non-English and non-Chinese language and 6 others) were excluded. At last, 9 literatures lacking complete data and one reporting other SNV variation were excluded. A total of 18 eligible literatures were finally enrolled (7, 8, 11–18). Searching procedures were listed in Figure 1.

18 eligible literatures were published from 2003 to 2018, and 10 were published in English (1, 7–9, 11–13, 15, 16, 19), and the remaining were published in Chinese language (18, 20–25). According to the study endpoints, 4 literatures reported acute coronary syndrome (ACS), 3 reported coronary atherosclerosis (CA), 2 reported CAD, 7 reported myocardial infarction (MI), and one was sub grouped into CAD and MI.

Research characteristics

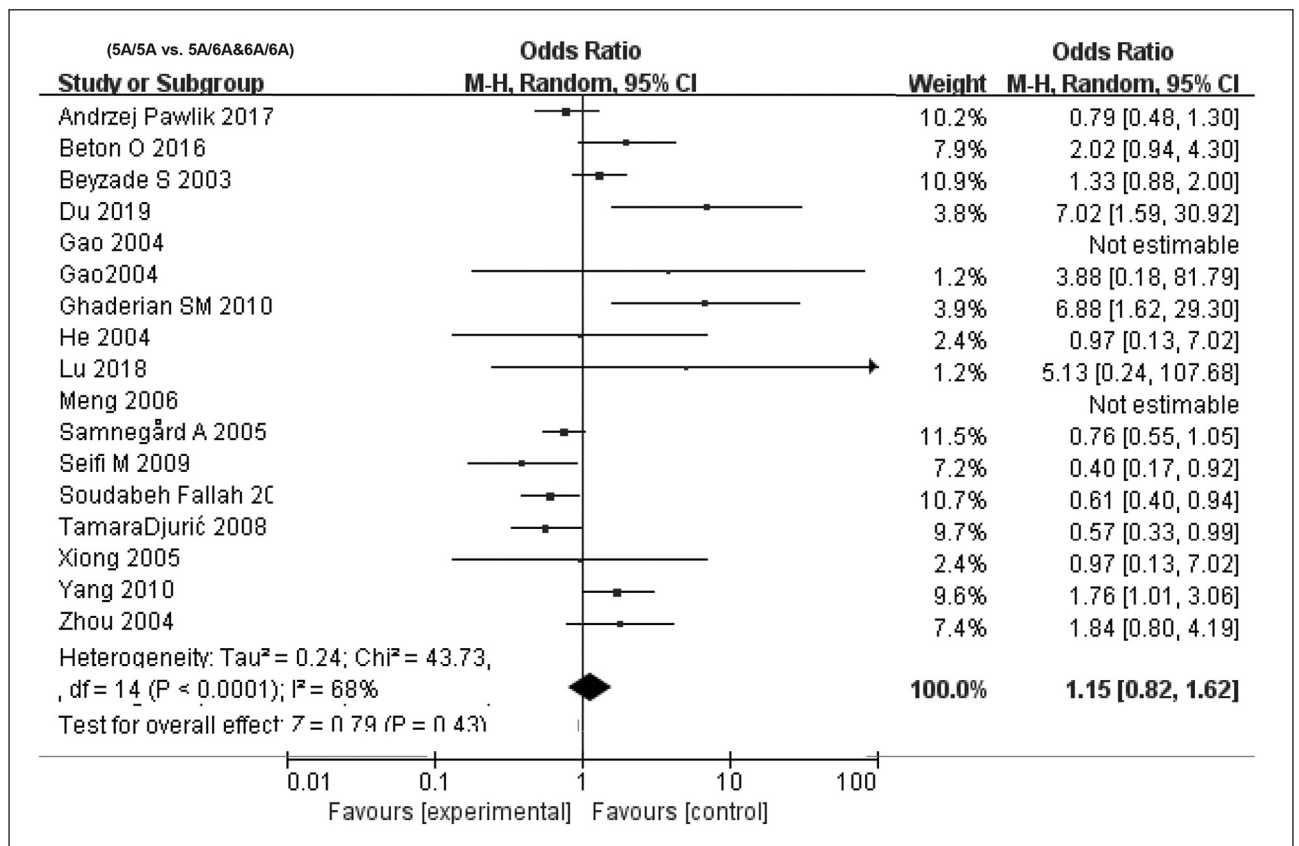
Among the 18 eligible literatures, 5 were conducted in Caucasian population (7, 12, 14, 15, 19), 8 were in East Asian population (mainly Chinese population) (17, 18, 20–25), and 4 were in Middle East population (8, 11, 13, 19). Patients and controls were all hospital-based population, except for four literatures that did not identify resource of controls. Genotype distribution of controls was in accordance to HWE ($P_{\text{HWE}} > 0.05$). Detailed information was listed in Table I.

Overall relevance

Four genetic models were applied for analyzing the involvement of MMP3 -1612 5A/6A in CAD. Heterogeneity existed in every model ($I^2 > 50\%$, $P < 0.05$), and thus the random-effects model was used for calculating pooled OR. In recessive model (OR=1.3, 95% CI=1.2–1.64, $P=0.03$) and over-dominant model (OR=1.50, 95% CI=1.14–1.97, $P=0.002$), MMP3 -1612 5A/6A was correlated to susceptibility of CAD. In the allele model (OR=1.24, 95% CI=1.00–1.54, $P=0.05$), MMP3 -1612 5A/6A exerted a marginal effect on CAD. After excluding literatures close to HWE violation ($P=0.05$), no significant changes on overall estimates were observed (Figure 2, 3 and 4). Egger's test clarified no significant difference in publication bias in the four models ($P > 0.05$, data not shown). To further elucidate the

Table 1 Baseline characteristics of enrolled literatures.

	Author	Year	Country	Journal name/ publication origin	Genotyping methods	SNP loci (PHWE)	Sample size	Control	Sample
ACS									
	Andrzej Pawlik et al (14)	2017	Poles	IUBMB Life	PCR-RFLP	-1612 5A/6A (PHWE=0.26)	197 (male=142, female=55)	144 (male=103, female=41)	Blood
	He et al (22)	2004	China	Chin J Emerg Med	PCR-RFLP	-1612 5A/6A (PHWE=0.78)	103 (male=73, female=30)	100 (male=67, female=33)	
	Xiong et al (25)	2005	China	Chinese J Clin Rehabilitation	PCR-RFLP	-1612 5A/6A (PHWE=0.78)	103 (male=73, female=33)	100 (male=67, female=33)	
	Yang et al (18)	2010	China	J Tongji University	PCR	-1612 5A/6A (PHWE=0.06)	270 (male=184, female=86)	258 (male=162, female=96)	
CA									
	Tamara Djurić et al (12)	2008	Serbia	Clin Biochem	PCR	-1612 5A/6A (PHWE=0.19)	265 (male=158, female=107)	250 (male=142, female=108)	Blood

**Figure 2** Forest plots demonstrating the association between MMP3 -1612 6A / 5A polymorphism and CAD infection susceptibility in the different models: (5A/5A vs. 5A/6A&6A/6A).

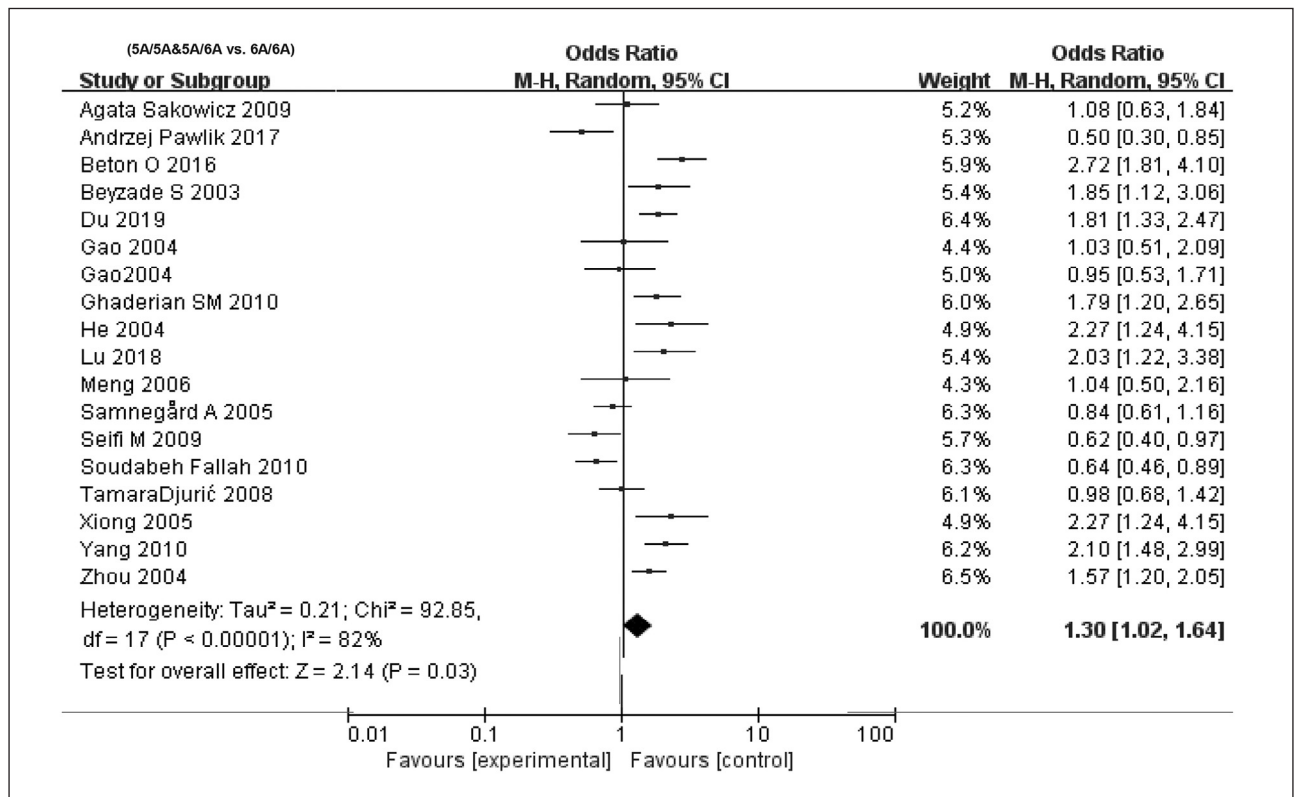


Figure 3 Forest plots demonstrating the association between MMP3 -1612 6A/5A polymorphism and CAD infection susceptibility in the different models: (5A/5A&5A/6A vs. 6A/6A).

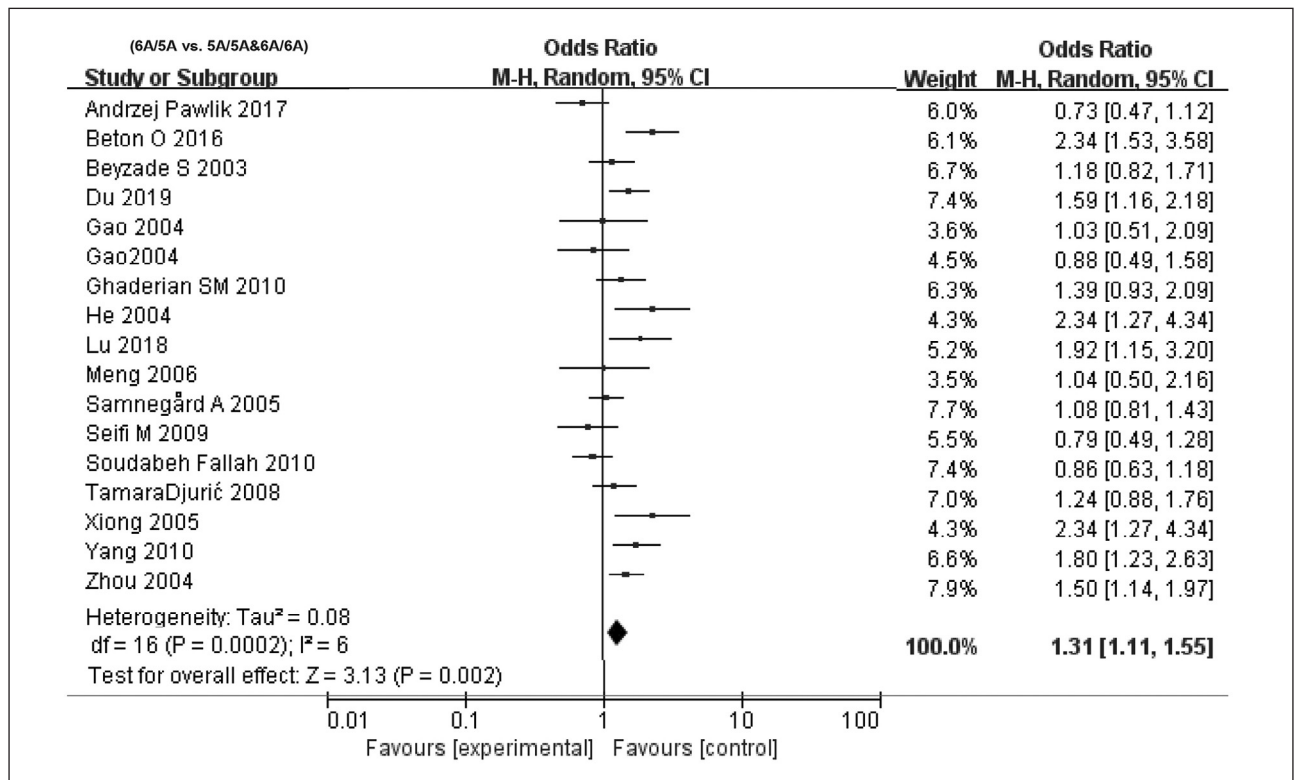


Figure 4 Forest plots demonstrating the association between MMP3 -1612 6A/5A polymorphism and CAD infection susceptibility in the different models: (6A/5A vs. 5A/5A&6A/6A).

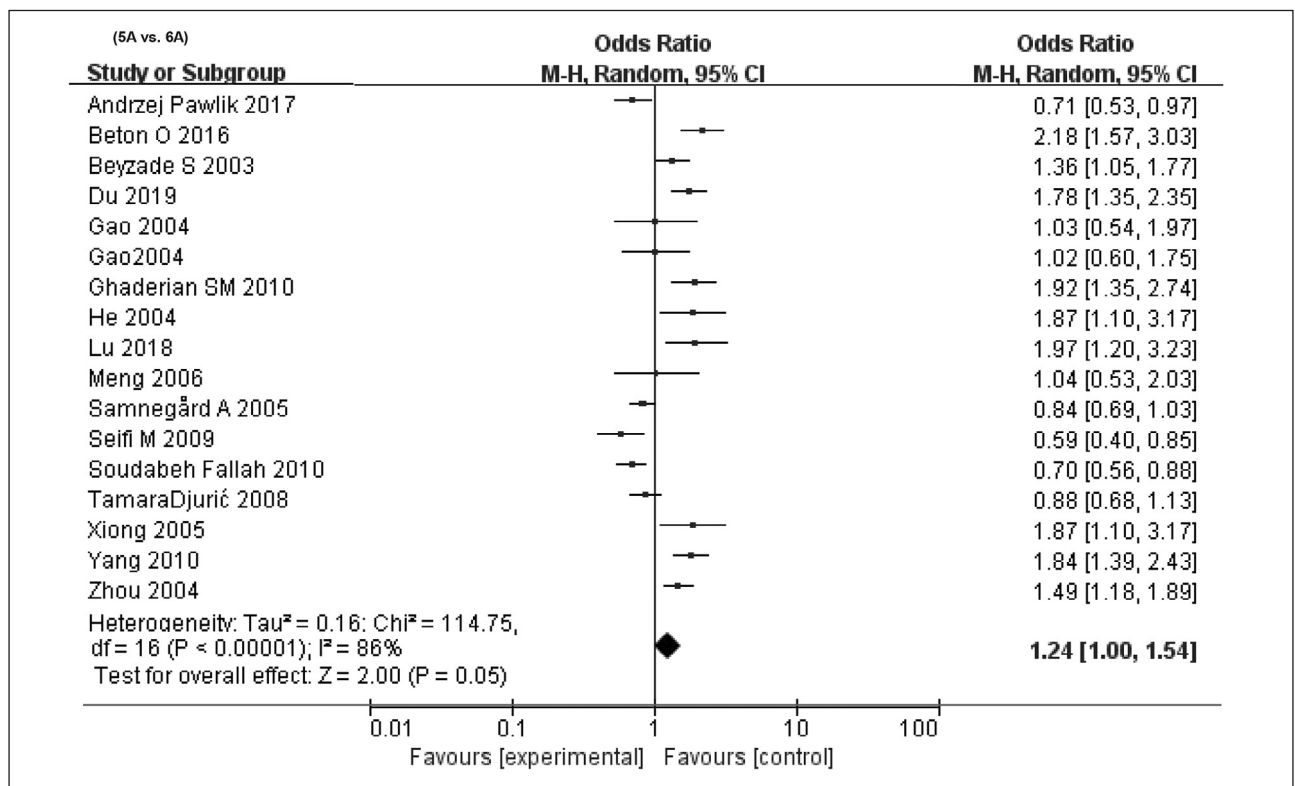


Figure 5 Forest plots demonstrating the association between MMP3 -1612 6A/5A polymorphism and CAD infection susceptibility in the different models: (5A vs. 6A).

Table II Subgroup analysis based on population.

Regions	Studies (case/controls)	Dominant model		Recessive model		Over-dominant model		Allele model	
		OR (95% CI); P-Value	I ² (PX ²)	OR (95% CI); P-Value	I ² (PX ²)	OR (95% CI); P-Value	I ² (PX ²)	OR (95% CI); P-Value	I ² (PX ²)
Caucasian	5 (968/1559)	0.84 (0.60, 1.17); 0.31	58% (0.07)	0.94 (0.61, 1.45); 0.77	77% (0.005)	1.06 (0.87, 1.30); 0.57	26% (0.25)	0.92 (0.72, 1.19); 0.53	75% (0.007)
East Asian	9 (1838/1842)	1.94 (1.29, 2.93); 0.002	0% (0.59)	1.68 (1.40, 2.02); <0.00001	31% (0.17)	1.57 (1.31, 1.88); <0.00001	26% (0.22)	1.60 (1.39, 1.84); <0.00001	14% (0.32)
Middle Eastern	4 (1095/913)	1.18 (0.44, 3.12); 0.75	84% (0.0003)	1.31 (0.70, 2.47); 0.40	91% (<0.00001)	1.22 (0.76, 1.97); 0.42	82% (0.0007)	1.14 (0.60, 2.19); 0.60	94% (<0.00001)

potential factors that may lead to heterogeneity, subgroup analyses were conducted.

Subgroup analysis based on population

Heterogeneity was absent in four genetic models analyzing the involvement of MMP3 -1612 5A/6A in CAD in East Asian population ($I^2 < 50\%$, $P > 0.05$). Mainly in Chinese population, MMP3 -1612 5A/6A gene polymorphism was remarkably linked to CAD

($P < 0.05$, $OR > 1$). Unlikely, no relationship between MMP3 -1612 5A/6A and CAD was observed in Caucasian population and Middle East population ($P > 0.05$). In particular, heterogeneity existed in recessive genetic model ($I^2 = 77\%$) and allele model ($I^2 = 75\%$) in Caucasian population, as well as four genetic models in Middle East population ($I^2 > 50\%$, $P < 0.05$) (Table II).

Table III Subgroup analysis based on endpoints.

Outcomes	Studies (case/controls)	Dominant model		Recessive model		Over-dominant model		Allele	
		OR (95% CI); P-Value	I ² (PX ²)	OR (95% CI); P-Value	I ² (PX ²)	OR (95% CI); P-Value	I ² (PX ²)	OR (95% CI); P-Value	I ² (PX ²)
ACS	4 (673/602)	1.13 (0.67, 1.89); 0.64	33% (0.21)	1.52 (0.75, 3.11); 0.25	87% (<0.0001)	1.60 (0.90, 2.82); 0.11	81% (0.001)	1.44 (0.83, 2.49); 0.19	88% (<0.0001)
CA	3 (760/763)	0.56 (0.41, 0.77); 0.0004	0% (0.67)	1.36 (0.49, 3.81); 0.56	90% (<0.0001)	0.96 (0.74, 1.26); 0.79	36% (0.21)	0.73 (0.59, 0.90); 0.004	43% (0.17)
CAD	3 (451/494)	2.13 (1.02, 4.44); 0.04	0% (0.56)	1.91 (1.15, 3.16); 0.01	63% (0.07)	1.29 (1.12, 1.49); 0.007	48% (0.15)	1.77 (1.19, 2.63); 0.005	52% (0.13)
MI	7 (2017/2455)	1.87 (0.98, 3.56); 0.06	76% (0.001)	1.38 (1.06, 1.80); 0.02	67% (0.006)	1.31 (1.11, 1.55); 0.0006	10% (0.35)	1.24 (1.00, 1.54); 0.04	80% (<0.0001)

Subgroup analysis based on endpoints

MMP3 -1612 5A/6A was significantly linked to CAD under the four genetic models (dominant genetic model: $P=0.04/OR=2.13$; recessive genetic model: $P=0.01/OR=1.91$; over-dominant genetic model: $P=0.007/OR=0.07$; allele model: $P=0.005/OR=1.17$) (Table III). In the meantime, heterogeneity existed in recessive genetic model ($I^2=63%$) and allele model ($I^2=52%$), and thus a random-effects model was applied. Compared with subjects carrying MMP3 -1612 6A allele homozygous, susceptibility to MI increased 38% in those carrying MMP3 -1612 6A allele heterozygote (1.06–1.80, 0.02), which increased 31% in those carrying MMP3 -1612 5A/6A allele heterozygote (1.11–1.55, 0.0006) (Table III). A similar association was observed in the allele model of MMP3 -1612 5A/6A. Nevertheless, the individual estimates of risk assessment were heterogeneous, and the possibility of publication bias was also high.

Discussion

MMPs are a family of Zn²⁺-dependent neutral proteases that degrade and reshape ECM, thus maintaining their homeostasis (26). MMP3 has a proteolytic activity on many ECM macromolecules (including different types of collagen) and it is able to promote the transformation of other MMPs. It is reported that MMP1 is upregulated in human atherosclerotic plaques, and ECM degradation activity is also enhanced, suggesting the involvement of MMP1 in CAD and MI (26, 27). A common deletion/insertion polymorphism (rs3025058) exists in promoter region of human MMP3, which is characterized as 5 or 6 adenosines at 1612 bp upstream of transcription initiation site (28). Multiple studies have reported that MMP3 rs3025058 is closely linked to coronary atherosclerotic diseases (29–31).

Previous studies generally believed that MMP3 5A/6A is associated with AS, and the 5A allele is associated with plaque rupture. In this paper, CAD risk in subjects carrying MMP3 -1612 5A homozygous was 30% higher than those carrying MMP3 -1612 6A homozygous. In over-dominant genetic model, MMP3 -1612 5A/6A was a risk factor for CAD. Inconsistent with our findings, a relevant study reported that morbid risk and progression risk are higher in subjects carrying MMP3 -1612 6A homozygous than those carrying MMP3 -1612 5A homozygous (32). Xu et al. (33) suggested that MMP3 and MMP9 mutations could be utilized as hallmarks for predicting susceptibility to CAD.

Furthermore, subgroup analyses uncovered that MMP3 -1612 6A/5A posed a huge impact on MI or East Asian population, which was consistent with the findings proposed by Want et al. (34) and Niu et al. (4). Moreover, taken into consideration of CAD as endpoint, MMP3 -1612 6A/5A was significantly related to CAD.

Some limitations in this analysis should be highlighted. First of all, MMP3 gene polymorphism could be interacted with other known or unknown CAD-associated risk factors. Secondly, we have ruled out many relevant literatures because genotype distribution was failed to be calculated using the inadequate data. Thirdly, sample size was relatively small. Fourthly, additional analyses on baseline characteristics of CAD patients were lacked.

Conclusions

Collectively, our findings demonstrated that MMP3 -1612 6A /5A was involved in CAD under recessive model and over-dominant model. In East Asian population (mainly Chinese population), MMP3 -1612 6A /5A was susceptibility to CAD in the four genetic models. Our findings required to be validated in a multi-center hospital with larger sample size.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Not applicable.

Funding

Not applicable.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

References

- Li GM, Zhang CL, Rui RP, Sun B, Guo W. Bioinformatics analysis of common differential genes of coronary artery disease and ischemic cardiomyopathy. *Eur Rev Med Pharmacol* 2018; 22(11): 3553–69.
- Ershow AG, Brown LM, Cantor KP. Intake of tapwater and total water by pregnant and lactating women. *Am J Public Health* 1991; 81(3): 328–34.
- Sternlicht MD, Werb Z. How matrix metalloproteinases regulate cell behavior. *Annu Rev Cell Dev Bi* 2001; 17: 463–516.
- Johnson JL, Jackson CL, Angelini GD, George SJ. Activation of matrix-degrading metalloproteinases by mast cell proteases in atherosclerotic plaques. *Arterioscler Thromb Vasc Biol* 1998; 18(11): 1707–15.
- Mittal B, Mishra A, Srivastava A, Kumar S, Garg N. Matrix metalloproteinases in coronary artery disease. *Adv Clin Chem* 2014; 64: 1–72.
- Pleskovic A, Letonja MS, Vujkovic AC, Starcevic JN, Caprnda M, Curilla E, et al. Matrix metalloproteinase-3 gene polymorphism (rs3025058) affects markers atherosclerosis in type 2 diabetes mellitus. *Vasa* 2017; 46(5): 363–9.
- Beyzade S, Zhang S, Wong YK, Day IN, Eriksson P, Ye S. Influences of matrix metalloproteinase-3 gene variation on extent of coronary atherosclerosis and risk of myocardial infarction. *J Am Coll Cardiol* 2003; 41(12): 2130–7.
- Fallah S, Seifi M, Samadikuchaksaraei A. Risk of coronary artery stenosis in Iranian type 2 diabetics: is there a role for matrix metalloproteinase-3 gene (-1612 5A/6A) polymorphism? *J Physiol Biochem* 2010; 66(4): 359–64.
- Koch W, de Waha A, Hoppmann P, Schomig A, Kastrati A. Haplotypes and 5A/6A polymorphism of the matrix metalloproteinase-3 gene in coronary disease: case-control study and a meta-analysis. *Atherosclerosis* 2010; 208(1): 171–6.
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *Jama-J Am Med Assoc* 2000; 283(15): 2008–12.
- Beton O, Arslan S, Acar B, Ozbilum N, Berkan O. Association between MMP-3 and MMP-9 polymorphisms and coronary artery disease. *Biomed Rep* 2016; 5(6): 709–14.
- Djuric T, Zivkovic M, Radak D, Jekic D, Radak S, Stojkovic L, et al. Association of MMP-3 5A/6A gene polymorphism with susceptibility to carotid atherosclerosis. *Clin Biochem* 2008; 41(16–17): 1326–9.
- Ghaderian SM, Akbarzadeh NR, Tabatabaei PA. Genetic polymorphisms and plasma levels of matrix metalloproteinases and their relationships with developing acute myocardial infarction. *Coronary Artery Dis* 2010; 21(6): 330–5.
- Pawlik A, Plucinska M, Kopec M, Glabowski D, Czerewaty M, Safranow K. MMP1 and MMP3 gene polymorphisms in patients with acute coronary syndromes. *lubmb Life* 2017; 69(11): 850–5.
- Sakowicz A, Fendler W, Lelonek M, Pietrucha T. Genetic variability and the risk of myocardial infarction in Poles under 45 years of age. *Arch Med Sci* 2010; 6(2): 160–7.
- Seifi M, Fallah S, Firoozrai M. Influence of genetic polymorphism in matrix metalloproteinase-3 on extent of coronary atherosclerosis and risk of coronary artery stenosis. *Arch Med Res* 2009; 40(7): 600–4.
- Zhou X, Huang J, Chen J, Su S, Chen R, Gu D. Haplotype analysis of the matrix metalloproteinase 3 gene and myocardial infarction in a Chinese Han population. The Beijing atherosclerosis study. *Thromb Haemostasis* 2004; 92(4): 867–73.
- Liu PY, Li YH, Chan SH, Lin LJ, Wu HL, Shi GY, et al. Genotype-phenotype association of matrix metalloproteinase-3 polymorphism and its synergistic effect with smoking on the occurrence of acute coronary syndrome. *Am J Cardiol* 2006; 98(8): 1012–7.
- Samnegard A, Silveira A, Lundman P, Boquist S, Odeberg J, Hulthe J, et al. Serum matrix metalloproteinase-3 concentration is influenced by MMP-3 -1612 5A/6A promoter genotype and associated with myocardial infarction. *J Intern Med* 2005; 258(5): 411–9.
- Du JB, Liu Y, Gao J, et al. Correlation between promoter polymorphism and extracellular matrix stability of atherosclerotic plaques. *Chinese journal of medical genetics*. 2019; 36: 645–8.
- Gao B, Li ZC. Study on the relationship between plasma level of matrix metalloproteinase-3 and its promoter gene 5A/6A polymorphism and coronary heart disease.

- Chinese Critical Emergency Medicine 2004; 2004-09-10(09): 536–9.
22. He CY, Zhou X, Xiong Y, Wang L, Wu J, Yu H. Polymorphism analysis of mmp-3 gene promoter 5A/6A in patients with acute coronary syndrome. Chinese Journal of Emergency Medicine 2004; 13: 748–50.
23. Lu H, Hu S, Wang R, Peng W, Wang TT. Correlation between matrix metalloproteinase 3 gene polymorphism and coronary atherosclerotic heart disease in elderly patients. Journal of Clinical and Experimental Medicine 2018; 17: 1200–3.
24. Meng DM, MAO YM, Chen Q, Geng J, Qin L, Zhao BR, Zhao FM, Cui RZ. Relationship between matrix metalloproteinase gene polymorphism and coronary heart disease. Tianjin Medicine 2006; 34: 295–8.
25. Xiong Y, Wei XY, Yang XL, Wang L, He, Zhou Xin. Association of matrix metalloproteinase 3 and 12 gene polymorphism with the risk of acute coronary syndrome in han Chinese. Chinese Clinical Rehabilitation 2005; 9: 226–8.
26. Jones CB, Sane DC, Herrington DM. Matrix metalloproteinases: a review of their structure and role in acute coronary syndrome. Cardiovasc Res 2003; 59(4): 812–23.
27. Newby AC. Dual role of matrix metalloproteinases (matrixins) in intimal thickening and atherosclerotic plaque rupture. Physiol Rev 2005; 85(1): 1–31.
28. Ye S. Influence of matrix metalloproteinase genotype on cardiovascular disease susceptibility and outcome. Cardiovasc Res 2006; 69(3): 636–45.
29. Humphries SE, Martin S, Cooper J, Miller G. Interaction between smoking and the stromelysin-1 (MMP3) gene 5A/6A promoter polymorphism and risk of coronary heart disease in healthy men. Ann Hum Genet 2002; 66(Pt 5-6): 343–52.
30. Schwarz A, Haberbosch W, Tillmanns H, Gardemann A. The stromelysin-1 5A/6A promoter polymorphism is a disease marker for the extent of coronary heart disease. Dis Markers 2002; 18(3): 121–8.
31. Terashima M, Akita H, Kanazawa K, Inoue N, Yamada S, Ito K, et al. Stromelysin promoter 5A/6A polymorphism is associated with acute myocardial infarction. Circulation 1999; 99(21): 2717–9.
32. Bronić A, Ferenčak G, Bernat R, Leniček-Krleža J, Dumić J, Dabelić S. Association of fibrinogen and plasmin inhibitor, but not coagulation factor XIII gene polymorphisms with coronary artery disease. J Med Biochem 2021; 40 (2): 138–49.
33. Xu X, Wang L, Xu C, Zhang P, Yong F, Liu H, et al. Variations in matrix metalloproteinase-1, -3, and -9 genes and the risk of acute coronary syndrome and coronary artery disease in the Chinese Han population. Coronary Artery Dis 2013; 24(4): 259–65.
34. Wang J, Xu D, Wu X, Zhou C, Wang H, Guo Y, et al. Polymorphisms of matrix metalloproteinases in myocardial infarction: a meta-analysis. Heart 2011; 97(19): 1542–6.

Received: March 15, 2023

Accepted: April 01, 2023