INPLASY PROTOCOL

To cite: Lv et al. AGTR1rs5186 polymorphism is associated with the risk of restenosis after percutaneous coronary intervention:A meta-analysis. Inplasy protocol 2022110054. doi: 10.37766/inplasy2022.11.0054

Received: 11 November 2022

Published: 12 November 2022

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Support: **81873486, BE2022754, SZYQTD20210.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

AGTR1rs5186 polymorphism is associated with the risk of restenosis after percutaneous coronary intervention:A meta-analysis

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Review question / Objective: **Progress has been made in genetic investigations on restenosis for the past 20 years, many studies regarding AGTR1 rs5186 polymorphism and restenosis after percutaneous coronary intervention (PCI) have been published, but the result remains controversial. The study aimed to explore the relationship between rs5186 polymorphism and the risk of restenosis after PCI.**
Condition being studied: **Coronary atherosclerotic heart disease (CHD) is one of the major Cardiovascular disease. In addition to medical therapy, percutaneous coronary intervention (PCI) has become an important treatment for CHD. Primary PCI modalities include percutaneous transluminal coronary balloon angioplasty, coronary stenting. Which reduce CHD related mortality significantly. However, the disadvantages of coronary restenosis after PCI have become increasingly obvious. The pathophysiological of restenosis after PCI is damage to vascular endothelial cells, leading to hyperplasia of the neovascular endothelium. Angiotensin II in the renal angiotensin aldosterone system (RAAS) would stimulate the expression of smooth muscle cell growth factor to promote smooth muscle cell hyperplasia, migration, and thus the occurrence of restenosis. With the rapid development of sequencing technology, much progress has been made in genetic investigations on restenosis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 November 2022 and was last updated on 12 November 2022 (registration number INPLASY2022110054).

INTRODUCTION

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METHODS

Search strategy: This meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statements.

Participant or population: Patients after percutaneous coronary intervention (PCI).

Intervention: Patients with restenosis after PCI.

Comparator: Patients with no restenosis after PCI.

Study designs to be included: Case-control studies

Eligibility criteria: Studies meeting the following criteria were included: (1)Case-control studies;(2) Investigating the association of the rs5186 polymorphism and risk of restenosis; (3)Studies had data of odds ratios (ORs) and 95% confidence intervals(95% CI) or had sufficient data to calculate it.1) Case-control stu Investigating the association of the rs5186 polymorphism and risk of restenosis; (3)Studies had data of odds ratios (ORs) and 95% confidence intervals(95% CI) or had sufficient data to calculate it.

Information sources: the PubMed, Web of Science, Embase, CNKI, and Wan Fang databases.

Main outcome(s): The meta-analysis indicated a significant association between AGTR1 rs5186 polymorphism and restenosis after PCI. allelic (OR: 1.31, 95% CI:1.17-1.47, P<.001), homozygous (OR: 1.90, 95% CI: 1.50-2.44, P<0.001), heterozygous (OR: 1.10, 95% CI: 0.93-1.29, P=0.27), recessive (OR: 1.80, 95% CI:1.37-2.36, P<0.001), dominant genetic model (OR: 1.24, 95% CI: 1.06-1.44, P=0.006) in the whole population.

Quality assessment / Risk of bias analysis: we computed Egger test and drew the Begg funnel plot to estimate the publication bias. We could see that all 8 studies were distributed on 2 sides of the Begg funnel plot, which implied no publication bias in our meta-analysis.

Strategy of data synthesis: This meta-analysis was performed using Stata version 14.0. We did Hardy-Weinberg equilibrium (HWE) tests for every study included. We explored the associations between rs5186 polymorphism and risk of restenosis by combining ORs and 95% CIs under a random-effect or fixed model. A random-effects model for pooled analysis would be adopted when I2 >50% indicating heterogeneity. Otherwise, the fixed-effect model would be used. We also performed subgroup analyses to identify the underlying heterogeneity according to ethnicity, study sample size, PCI type. The analyses were conducted in 5 genetic models: allele (A allele distribution frequency of rs5186 polymorphism), homozygote model (AA vs. CC), heterozygote model (AC vs. AA), recessive model (CC vs. AC+ AA) and dominant model (CC+ CC vs. AA). Sensitivity analysis

was performed to evaluate the stability of the results. We investigated publication bias by calculating Egger test and drawing Begg funnel plot.

Subgroup analysis: In the subgroup analyses by ethnicity (Fig. 3), the association grew stronger with higher ORs in Asian under all genetic models: allelic (OR: 1.89, 95% CI: 1.48–2.40, P<.001), homozygous (OR: 3.35, 95% CI: 1.99-5.64, P <0.001), heterozygous (OR: 1.42, 95% CI: 1.02-1.98, P=0.04), recessive (OR: 2.89, 95% CI: 1.75-4.78, P <0.001), dominant genetic model (OR: 1.76, 95% CI: 1.30-2.38, P<0.001).In the Caucasian subgroup, we also found association under allelic (OR: 1.18, 95% CI: 1.03-1.34, P=0.02), homozygous (OR: 1.58, 95% CI: 1.19-2.09, P=0.002) recessive (OR: 1.59,95% CI:1.21-2.09, P=0.01). In summary, our meta-analysis suggested that rs5186 polymorphism in the AGTR1 gene increased the risk of restenosis after PCI, particularly in Asian, We also carried on subgroup analyses according to sample size, PCI type. The detailed information was presented in Table 4. Similar association was observed in both sample size (≥400) and PCI type(stent) subgroups that rs5186 polymorphisms in the AGTR1 gene increased the risk of restenosis after PCI.

Sensitivity analysis: We carried on the sensitivity analysis to find whether the omission of each study will change the pooled ORs quantitatively. No changed results are shown after the individual study was omitted in Figure 4, which supplied evidence to prove the increased risk of the rs5186 polymorphism to restenosis after PCI.

Language restriction: No.

Country(ies) involved: China (Dushu Lake Hospital Affiliated to Soochow University).

Keywords: Cardiovascular disease; rs5186; percutaneous coronary intervention; polymorphism.

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