



Review Article

Genetic Variations in microRNA and their Association with Coronary Artery Disease: A Comprehensive Meta-Analysis

Praveen Kumar Chandra Sekar^{ID}, Ramakrishnan Veerabathiran^{ID}

Human Cytogenetics and Genomics Laboratory, Faculty of Allied Health Sciences, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Tamil Nadu, India

Article info

Article History:

Received: May 21, 2025

Revised: October 16, 2025

Accepted: May 9, 2026

epublished: September 1, 2026

*Corresponding Author:

Ramakrishnan Veerabathiran,
Email: rkgenes@gmail.com

Abstract

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide, with genetic and molecular mechanisms playing a crucial role in its development. Among these, microRNAs (miRNAs) are important post-transcriptional regulators that affect endothelial function, inflammation, and lipid metabolism. This meta-analysis aimed to assess the association between four common miRNA polymorphisms, miR-146a (rs2910164), miR-149a (rs2292832), miR-196a2 (rs11614913), and miR-499 (rs3746444) and susceptibility to CAD. Relevant studies published up to 2025 were systematically collected from PubMed, Embase, and Google Scholar following PRISMA guidelines. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were calculated under various genetic models using either random- or fixed-effects models depending on heterogeneity. A total of 13,229 CAD cases and corresponding controls were included. The results indicated that miR-146a, miR-196a2, and miR-499 polymorphisms were significantly linked to CAD risk, especially among Asian populations, while miR-149a showed no overall association. Sensitivity analyses confirmed the stability of these findings, although moderate heterogeneity was observed in some models. Publication bias was evaluated using Begg's funnel plot and Egger's test, showing no significant asymmetry. These findings suggest that specific miRNA variants may play a role in CAD pathogenesis by modifying gene expression related to vascular inflammation and remodeling. However, due to the observed heterogeneity and limited data in certain ethnic groups, these associations should be interpreted with caution. Further large-scale, multiethnic studies are necessary to confirm these results and better understand the underlying molecular mechanisms.

Keywords: microRNA, Coronary artery disease, Polymorphism, Genetics

Introduction

Coronary artery disease (CAD) is a prevalent condition that frequently affects middle-aged and elderly individuals worldwide.¹ The cause of CAD is not fully understood. As people live longer, the number of CAD cases is increasing in developing countries such as India, and the WHO predicts that CAD will become the foremost cause of death globally in the near future.² Traditional factors such as smoking, alcohol consumption, obesity, overweight, hypertension, type 2 diabetes mellitus (T2DM), and hyperlipidemia have all been linked to an increased risk and progression of CAD.³⁻⁷ However, further research is required to determine the potential susceptibility factors that promote CAD development. An increasing number of molecular epidemiological studies have indicated that genetic factors may contribute to CAD susceptibility.^{8,9} However, genetic susceptibility to this disease remains unknown.¹⁰ Several single-nucleotide polymorphisms (SNPs) have shown a strong correlation with CAD susceptibility.¹¹

Among these variables, genetic variants, particularly those of microRNAs, have been identified as key contributing factors to CAD. miRNAs are a class of short

non-coding RNA comprising 22 nucleotides in length. They play a significant role in molecular mechanisms and cellular processes, particularly in human diseases such as diabetes, cancer, and cardiovascular conditions.^{12,13} Research indicates that miRNAs are essential for controlling biological processes involved in CAD.¹⁴ Furthermore, studies have demonstrated that miRNAs play a role in preventing oxidative stress, inflammation, energy metabolism, and smooth muscle cell proliferation, all of which are associated with the development of CAD.¹⁵

Variations in SNPs found in pre-miRNAs, as well as in specific miRNA-binding sites in target genes, can affect the interaction between particular miRNAs and mRNA target sites. This can potentially lead to the abnormal expression of these genes.¹⁶ As miRNAs play a role in regulating translation, genetic miRNA SNPs are believed to be implicated in the development of susceptibility to CAD. Previous studies have concentrated on the link between CAD development and several common miRNA SNPs, such as miR-146a rs2910164 C>G, miR-149a rs2292832, miR-196a2 rs11614913 T>C, and miR-499 rs3746444 A>G,^{17,18} but the results have been inconsistent. To rectify



these disparities, we performed an exhaustive assessment of all pertinent research to examine the correlation between these genetic variants and the risk of having CAD.

Methods

The research adhered to the standards set forth by the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA 2021) and the Meta-analysis on Genetic Association Studies Checklist. The study review protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) under registration ID CRD420565596, which can be accessed at <https://www.crd.york.ac.uk/PROSPERO/view/CRD420565596>, thereby ensuring transparency and reliability of the research.

Ethical consideration

Ethical approval was unnecessary as this study utilised existing published case-control studies. Due to the nature of this meta-analysis, patient consent forms were not required.

Study selection

The terms “coronary artery disease,” “microRNAs” (miR), and “polymorphism” (SNP) were used to search Google Scholar, PubMed, and Embase electronic databases. We systematically constructed search strings using controlled vocabulary (MeSH and Emtree terms) and Boolean operators to identify relevant studies. The search strategy combined terms related to genetic variation (“polymorphism” OR “single nucleotide polymorphism” OR “SNP”), disease outcomes (“coronary artery disease” OR “ischemic heart disease” OR “myocardial infarction”), and molecular targets (“microRNA” OR “miR” OR “micro-RNA”), along with specific rs IDs. The detailed search queries for each database are given in Supplementary Table S1. After selecting seven genes (miR-31, miR-143, miR-145, miR-146a, miR-149, miR-196a2, and miR-499), we subsequently narrowed our focus to a meta-analysis of publications that investigated miR-146a, miR-149, miR-196a2, and miR-499. These four miRNAs were included because they had sufficient independent case-control studies reporting complete genotype frequency data, allowing reliable pooled analysis. The remaining miRNAs (miR-31, miR-143, and miR-145) were excluded due to the inadequate number of eligible studies and insufficient data for meta-analysis. All retrieved citations were imported into EndNote X9 (Clarivate Analytics) for organization. Duplicate records were identified and removed using the software’s automated duplicate detection tool based on title, author, and DOI information. A manual verification step was also performed to ensure that overlapping datasets or repeated publications from the same research groups were excluded.

The criteria for determining the studies that could be included in a meta-analysis of CAD were clearly defined. The main requirement was that the studies had to be case-control studies that included genotyping of both healthy controls and patients with clinically confirmed

CAD. Additionally, studies had to involve individuals whose genetic variants were confirmed using RT-PCR or PCR-RFLP validation methods. Only articles published in English were included in this study.

Various exclusion criteria were applied to ensure the quality and relevance of the chosen studies. Studies with irrelevant designs, such as reviews and meta-analyses, were excluded. Duplicate articles were systematically identified and eliminated to prevent data double-counting. Studies of substandard quality that failed to meet set standards were omitted from consideration. Furthermore, papers lacking the necessary data for inclusion were omitted. Studies that failed to sufficiently control for potential confounding variables were eliminated to ensure the validity of the findings. Ultimately, non-human studies, including those involving animals or in vitro models, were omitted unless they were directly pertinent to the research subject.

Data extraction

Data extraction was conducted independently by two authors (PKCS and RV). All disputes were addressed through dialogue to achieve consensus. The analysis yielded comprehensive information encompassing the first author, study type, nation, publication year, sample size, sample characteristics, patient count, and genotyping methods.

Quality assessment

The methodological quality of the included case-control studies was evaluated using the Newcastle–Ottawa Scale (NOS),¹⁹ which evaluates studies based on three domains: selection of participants, comparability of cases and controls, and ascertainment of exposure. Studies scoring 7–9 points were considered high quality, 4–6 points moderate quality, and 0–3 points low quality. In addition, the Hardy–Weinberg equilibrium (HWE) p-value was calculated for the control groups to ensure genetic balance and data reliability. We employed the Robvis software to categorise these research based on their risk levels: high risk, uncertain risk with concerns, or low risk, reflecting the degree of danger involved with each study.

Statistical analysis

The present study aimed to examine the relationship between CAD and specific genetic variations in miR-146a, miR-149, miR-196a2, and miR-499. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to assess the strength of the association, with statistical significance set at $P < 0.05$. Heterogeneity among studies was evaluated using Cochran’s Q test and quantified through the I^2 statistic, where values around 25%, 50%, and 75% indicated low, moderate, and high heterogeneity, respectively. When heterogeneity was low ($I^2 < 50\%$), a fixed-effects model was employed; for significant heterogeneity ($I^2 \geq 50\%$), a random-effects model was used to provide a more conservative pooled estimate that considers both within- and between-study variances. Publication bias was assessed with Begg’s funnel plot and Egger’s regression test, with $P < 0.05$ suggesting potential

bias. Visual inspection of the funnel plot was performed to detect asymmetry. Statistical analyses were conducted using Review Manager version 5.4 and Cochrane ROB Tool 2.

Subgroup Analysis

To further explore potential sources of heterogeneity, two subgroups were pre-specified before the data synthesis. The first subgroup analysis was performed based on ethnicity to evaluate possible population-specific genetic effects on CAD susceptibility. This categorization was chosen because genetic variant frequencies and environmental risk factors often differ between ethnic groups, potentially influencing disease associations. The second subgroup analysis was conducted according to genetic models, including allelic (A vs. G), dominant (AA + AG vs. GG), recessive (AA vs. AG + GG), and codominant models, to assess the influence of different inheritance patterns on the overall genetic association. Subgroup analyses were performed only when a minimum of two independent studies were available for each category. ORs and 95% CIs were calculated for each subgroup, and differences between subgroups were interpreted in the context of between-study heterogeneity (I^2 statistic) and statistical significance ($P < 0.05$).

Power Analysis

We conducted a post hoc power analysis of the pooled data using a 95% CIs and a significance level (α) of 0.05. Statistical power was assessed for the combined and individual sample sizes of case and control groups for each selected gene. The analysis was performed using G*Power 3.1, a widely used software for power estimation in genetic association studies, and cross-verified using the online tool available at <http://www.power-analysis.com/>. Assuming a moderate effect size (Cohen's $d = 0.3$), the total sample size across included studies provided an estimated power exceeding 80%, indicating adequate sensitivity to detect true correlation while minimizing the risk of Type

II errors. This refined analysis supports the statistical robustness of our meta-analytic results without overstating the magnitude of the effect size

Results

We identified 294 citations following our search. Following the examination of abstracts and titles, 165 papers were eliminated. Subsequently, we scrutinized the 129 complete texts meticulously. Ninety-nine were removed for multiple reasons: Of the total, 29 were reviews, 15 had distinct study aims, 13 concentrated on protein levels, and 12 were devoid of genotyping data (Figure 1). In total, 30 studies were incorporated (Table 1). Specifically, seven articles assessed miR-146a gene polymorphisms, five assessed miR-149, 11 assessed miR-196a2, and seven assessed miR-499 polymorphisms.

Risk bias

The quality of the chosen studies was evaluated using a comprehensive methodological assessment utilising the Cochrane Rob Tool 2, as seen in Figure 2. This figure illustrates that each row pertains to a distinct study, whereas each column denotes a certain sort of bias. Colour coding represents the reviewer's evaluation of bias risk for each analysis type: green indicates minimal bias potential, red signifies significant bias potential, and yellow denotes ambiguous bias risk. The findings indicated a significantly low risk of bias among the selected studies, suggesting that the research was well-designed, executed, and documented, hence effectively mitigating or eliminating potential biases or errors.

miR-146a polymorphism

miR-146a polymorphism has been extensively studied. A meta-analysis of seven studies, which included 1,727 CAD cases and 1,911 controls,²⁰⁻²⁶ revealed a substantial correlation in allelic ($P = 0.01$, OR = 1.53, 95% CI [1.09,

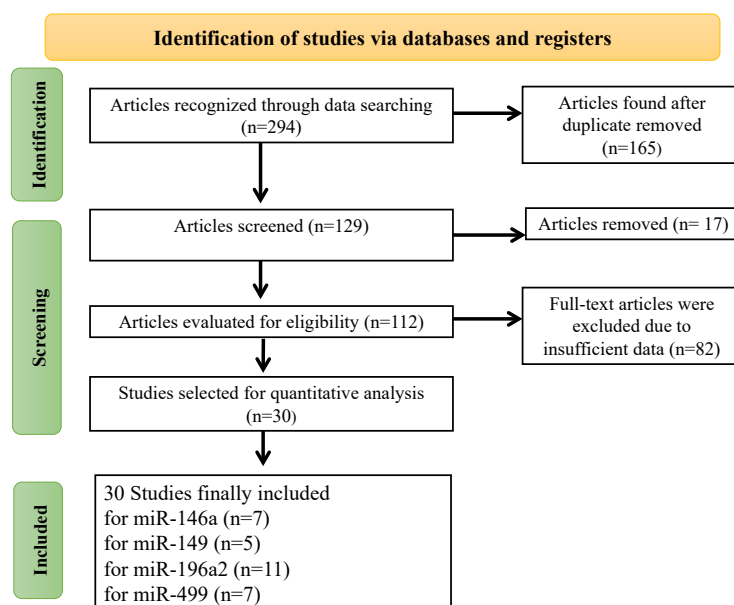


Figure 1. Flow diagram detailing a selection of studies for inclusion

Table 1. Characteristics of case-control studies included in the meta-analysis

First author	Year	Country/Ethnicity	Genotyping Method	Case /control	Genotype frequency						Allele frequency				HWE
					Case			Control			Case		Control		
miR-146a-rs2910164					GG	CG	CC	GG	CG	CC	G	C	G	C	
Fragoso ²⁰	2019	Mexico/ Caucasian	PCR-RFLP	218/595	116	85	17	277	267	51	317	119	821	369	0.233
Mehrjard ²¹	2022	Iran/Asian	PCR	297/306	133	128	36	150	121	35	394	200	421	191	0.166
Tie ²²	2023	Japan/Asian	PCR	93/58	13	60	20	2	16	40	86	100	20	96	0.799
Ali ²³	2022	Egypt/ Caucasian	RFLP-PCR	200/100	85	67	48	15	32	53	237	163	62	138	0.011
Qiao ²⁴	2023	China/Asian	PCR	619/552	109	302	208	73	263	216	520	718	409	695	0.614
Agiannitopoulos ²⁵	2020	Greece/Caucasian	RFLP-PCR	200/200	91	95	14	101	84	15	277	123	286	114	0.665
Mir ²⁶	2020	India/Asian	PCR-RFLP	100/100	11	51	38	5	40	55	73	127	50	150	0.504
miR-196a- rs11614913					TT	TC	CC	TT	TC	CC	T	C	T	C	
Fragoso ²⁰	2019	Mexico/ Caucasian	PCR-RFLP	218/588	38	113	67	87	266	235	189	247	440	736	0.409
Agiannitopoulos ²⁵	2020	Greece/Caucasian	RFLP-PCR	200/200	31	80	89	16	77	107	142	258	109	291	0.681
Chen ²⁷	2014	China/Asian	PCR-RFLP	777/889	312	450	15	322	406	161	1074	480	1050	728	0.01
Huang ²⁸	2015	China/Asian	PCR-RFLP	170/206	44	81	45	54	120	32	169	171	228	184	0.01
Qiu ²⁹	2019	China/Asian	PCR-RFLP	500/1106	163	247	90	335	576	195	573	427	1246	966	0.05
Sung ³⁰	2016	Korea/Asian	PCR-RFLP	522/535	179	236	107	153	274	108	594	450	580	490	0.464
UlHaq ³¹	2022	Pakistan/Asian	PCR-RFLP	80/80	16	40	24	11	19	50	72	88	41	119	0.0007
Xiong ³²	2014	China/Asian	PCR	225/283	86	131	8	83	132	68	303	147	298	268	0.277
Yang ³³	2012	China/Asian	TaqMan	1897/1838	493	971	433	528	921	389	1957	1837	1977	1699	0.733
Zhang ³⁴	2013	China/Asian	PCR-RFLP	233/349	75	117	41	135	164	50	267	199	434	264	0.986
Zhi ³⁵	2012	China/Asian	PCR-RFLP	916/584	291	470	155	208	278	98	1052	780	694	474	0.754
miR-149a-rs2292832					TT	TC	CC	TT	TC	CC	T	C	T	C	
Agiannitopoulos ²⁵	2020	Greece/Caucasian	PCR-RFLP	200/200	24	76	100	26	85	89	124	276	137	263	0.425
Qiu ²⁹	2019	China/Asian	PCR-RFLP	500/1106	163	247	90	335	576	195	573	427	1246	966	0.05
Sung ³⁰	2016	Korea/Asian	PCR-RFLP	522/535	227	248	47	263	219	53	702	342	745	325	0.456
Ghaffarzadeh ³⁶	2017	Iran/Asian	PCR-RFLP	272/149	53	124	95	17	79	53	230	314	113	185	0.123
Xu ³⁷	2009	China/Asian	PCR-RFLP	501/505	224	233	44	220	236	49	681	321	676	334	0.21
miR-499-rs3746444					AA	AG	GG	AA	AG	GG	A	G	A	G	
Qiu ²⁹	2019	China/Asian	PCR-RFLP	500/1106	5	138	357	27	279	800	148	852	333	1879	0.649
Sung ³⁰	2016	Korea/Asian	PCR-RFLP	522/535	9	155	358	13	168	354	173	871	194	876	0.181
Xiong ³²	2014	China/Asian	PCR-RFLP	295/283	227	65	3	212	67	4	519	71	491	75	0.616
Yang ³³	2012	China/Asian	TaqMan	827/923	589	210	28	683	212	28	1388	266	1578	268	0.023
Zhi ³⁵	2012	China/Asian	PCR-RFLP	916/584	629	201	86	396	167	21	1459	373	959	209	0.586
Labbaf ³⁹	2017	Iran/Asian	PCR-RFLP	288/150	68	142	78	48	77	25	278	298	173	127	0.529
Chen ⁴⁰	2017	China/Asian	Mass Array	421/464	264	110	47	342	103	19	638	204	787	141	0.002

2.15], $I^2 = 90\%$) or dominant ($P = 0.05$, OR = 0.68, 95% CI [0.45, 1.01], $I^2 = 80\%$). Similar results were observed in the homozygote ($P = 0.02$, OR = 0.50, 95% CI [0.28, 0.89, $I^2 = 81\%$]), recessive ($P = 0.01$, OR = 0.55, 95% CI [0.34, 0.89, $I^2 = 85\%$]), and heterozygote ($P = 0.02$, OR = 1.65, 95% CI [1.08, 2.53, $I^2 = 77\%$]) groups using the random effects model, as depicted in Figure 3. Subgroup analyses of Caucasian and Asian populations revealed that the dominant model of Asian populations showed a substantial correlation ($P = 0.05$, OR = 1.96, 95% CI [0.98, 3.94, $I^2 = 84\%$]), but not in the Caucasian population ($P = 0.2$, OR = 2.00, 95% CI [0.63, 6.30, $I^2 = 88\%$]) (Table 2).

miR-196a2 polymorphism

In 11 studies involving 5,738 CAD cases and 6,658 controls, the polymorphism of miR-196a2 was investigated.^{20,25,27-35} Based on a random effects model, the analysis revealed a substantial correlation between the G vs. A allele ($P = 0.05$, OR = 1.18, 95% CI [1.00, 1.39], $I^2 = 88\%$), homozygous ($P = 0.03$, OR = 0.62, 95% CI [0.40, 0.96], $I^2 = 92\%$), heterozygote ($P = 0.03$, OR = 1.57, 95% CI [1.05, 2.35, $I^2 = 93\%$]), and recessive ($P = 0.02$, OR = 0.64, 95% CI [0.43, 0.94, $I^2 = 93\%$]). However, no substantial correlation was observed in the dominant group ($P = 0.26$, OR = 0.92, 95% CI [0.79, 1.06], $I^2 = 63\%$) (Figure 4). Subgroup analyses of the Caucasian and Asian populations revealed that

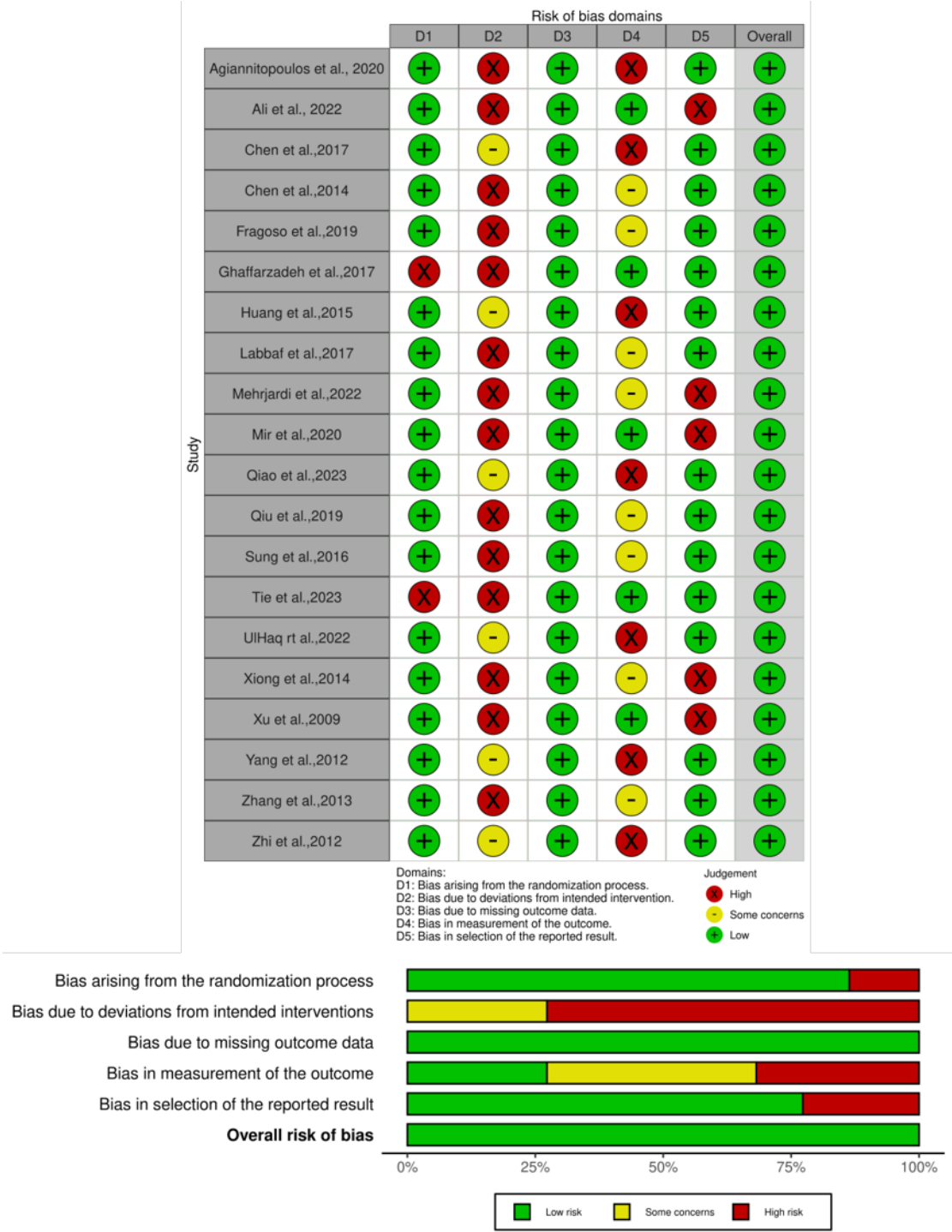


Figure 2. Risk of Bias summary and graph for investigating miR-146a, miR149a, miR-196a2, and miR-499 gene polymorphism

the dominant model of Asian populations showed a significant correlation ($P=0.01$, $OR=1.50$, 95% CI [1.07, 2.09], $I^2=94\%$) and in the Caucasian population ($P=0.04$, $OR=1.43$, 95% CI [0.96, 2.12], $I^2=84\%$) (Table 2).

miR-149a polymorphism

The miR polymorphism (-149a) was examined in five studies that comprised 1,995 patients and 2,495 controls.^{25,29,30,36,37} The fixed-effects model revealed no association in the allelic genetic ($P=0.96$, $OR=1.00$, 95% CI [0.92, 1.10], $I^2=9\%$), homozygous ($P=0.45$, $OR=0.93$, 95% CI [0.76, 1.13], $I^2=0\%$), the heterozygote GA vs. AA

($P=0.72$, $OR=0.97$, 95% CI [0.81, 1.15], $I^2=0\%$), and the recessive ($P=0.90$, $OR=1.01$, 95% CI [0.86, 1.19], $I^2=0\%$). Conversely, the random-effects model also revealed no association in the dominant group ($P=0.86$, $OR=0.99$, 95% CI [0.87, 1.13], $I^2=55\%$) (Figure 5).

miR-499 polymorphism

The analysis focused on the miR polymorphism (499 G/A) and included seven studies with 3,769 CAD cases and 4,045 controls.^{29,30,32,35,38-40} The random effects model showed a strong correlation for the G vs. A allele ($P=0.02$, $OR=0.83$, 95% CI [0.71, 0.91], $I^2=67\%$), dominant

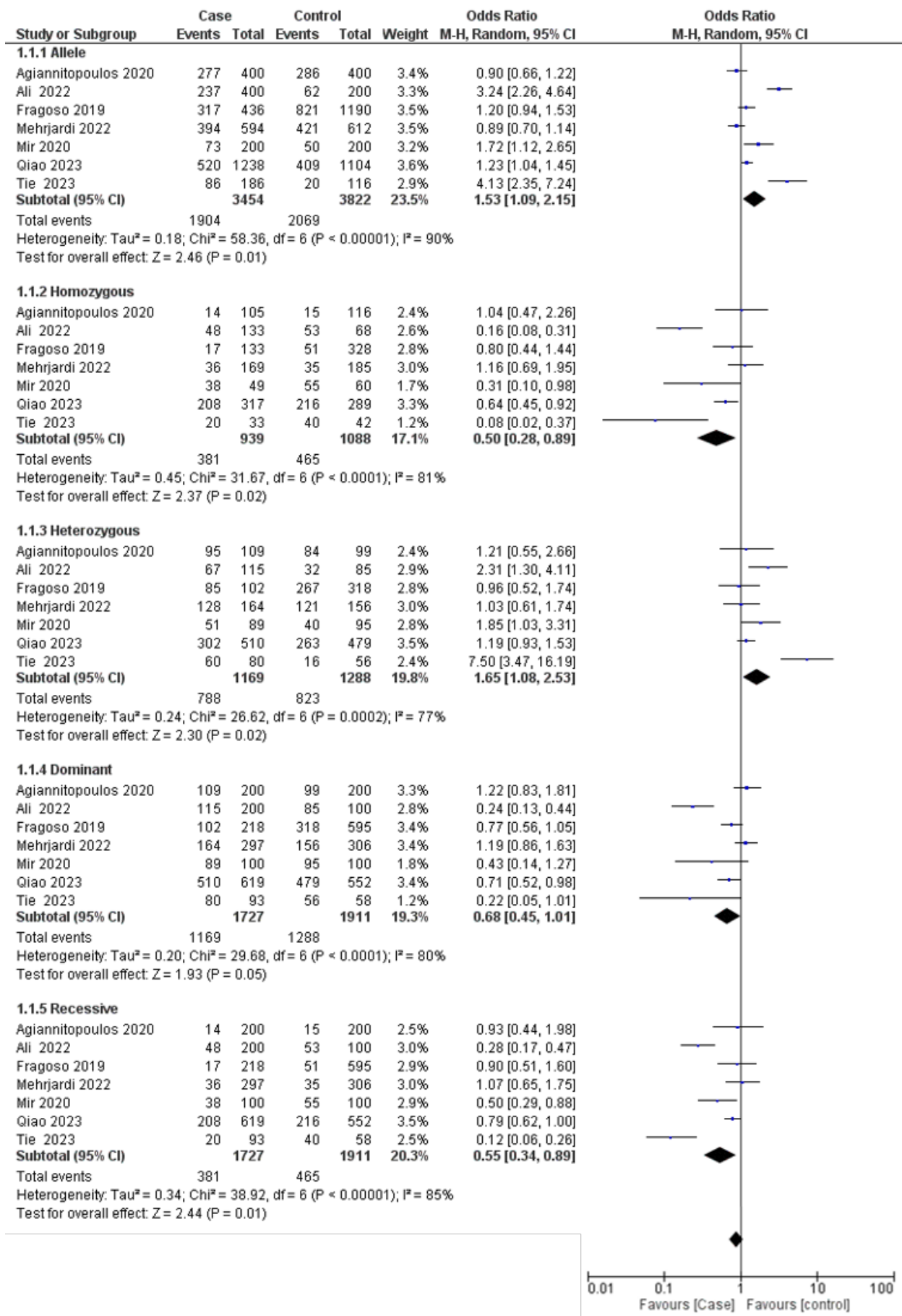


Figure 3. Forest plot showing an association between the miR-146a rs2910164 C>G gene polymorphism and CAD risk in the genetic models

Table 2. Subgroup analysis for miR-499 rs3746444 A>G, miR-146a rs2910164 C>G and miR-196a2 rs11614913 T>C gene polymorphisms with CAD risk

Polymorphism	Genetic Model	Ethnicity	Number of Studies	Test of association			Test of heterogeneity		I ²	Publication bias P (Egger's test)
				OR	95 % CI	P	Model	P		
miR-196a-rs11614913	Recessive model (GG vs. GA+AA)	Overall	11	1.0895	[0.9395; 1.2635]	0.256603	Random	0.0024	0.6329	0.0937
		Asian	9	1.0455	[0.9009; 1.2134]	0.557998	Random	0.0059	0.6282	0.3044
		Caucasian	2	1.2157	[0.8008; 1.8455]	0.359088	Fixed	0.1034	0.854	0.3123
	Dominant model (GG+GA vs. AA)	Overall	11	1.5684	[1.0682; 2.3028]	0.021637	Random	0	0.9273	0.0466
		Asian	9	1.6105	[1.0112; 2.5650]	0.044782	Random	0	0.9496	0.0904
		Caucasian	2	1.5004	[1.0768; 2.0904]	0.016509	Fixed	0.2127	0.84456	0.0079
miR-499-rs3746444	Recessive model (GG vs. GA+AA)	Overall	7	0.8079	[0.6514; 1.0020]	0.052116	Random	0.0225	0.5925	0.3138
		Asian	7	0.8079	[0.6514; 1.0020]	0.052116	Random	0.0225	0.5925	0.3138
	Dominant model (GG+GA vs. AA)	Overall	7	0.6655	[0.4649; 0.9526]	0.02605	Random	0.0001	0.7889	0.2369
		Asian	7	0.6655	[0.4649; 0.9526]	0.02605	Random	0.0001	0.7889	0.2369
miR-146a-rs2910164	Recessive model (GG vs. GA+AA)	Overall	7	1.4786	[0.9948; 2.1977]	0.053077	Random	0	0.7972	0.156
		Asian	4	1.3865	[0.8291; 2.3186]	0.212874	Random	0.0203	0.6941	0.2878
		Caucasian	3	2.2657	[0.7241; 7.0888]	0.159924	Random	0.0009	0.9087	0.0904
	Dominant model (GG+GA vs. AA)	Overall	7	1.8269	[1.1259; 2.9644]	0.014686	Random	0	0.8458	0.3321
		Asian	4	1.9692	[0.9825; 3.9465]	0.056095	Random	0	0.8844	0.351
		Caucasian	3	2.0046	[0.6371; 6.3079]	0.234416	Random	0.0028	0.8883	0.6941

($P=0.05$, OR = 1.24, 95% CI [1.00, 1.54], $I^2=59\%$), recessive ($P=0.031$, OR = 1.50, 95% CI [1.05, 2.15], $I^2=79\%$), and no association under the heterozygous ($P=0.06$, OR = 0.70, 95% CI [0.48, 1.01], $I^2=79\%$). In contrast, the fixed-effects model analysis revealed a strong correlation in the homozygous group ($P<0.0001$, OR = 1.98, 95% CI [1.41, 2.78], $I^2=42\%$) (Figure 6). Subgroup analyses of Asian populations revealed that the dominant model yielded a significant outcome ($P=0.002$, OR = 0.66, 95% CI [0.46, 0.85], $I^2=78\%$). (Table 2).

An examination of sensitivity analysis and publication bias

Egger's test and Begg's funnel plot were used in the study to evaluate publication bias in the literature. The research revealed no asymmetry in funnel plots for any of the five genetic models for the entire population. Furthermore, Begg's test results demonstrated an absence of publication bias for the polymorphisms of miR-146a, miR-149, miR-196a2, and miR-499. Significant asymmetry was noted in the included papers about these SNPs, which was further corroborated by Egger's linear regression tests. Nevertheless, the results remained statistically significant and robust (Figure 7). A sensitivity analysis was performed to assess the influence of each study on the overall results by methodically omitting individual studies and those that violated Hardy-Weinberg equilibrium. However, sensitivity analysis revealed that the omission of any individual study did not significantly affect the original results (Figure 8).

Power analysis

A power analysis was performed to assess the significance level of the selected SNPs for each study. Our research revealed that the sample sizes in the reviewed literature met

the required significance level, with an α -error probability of 0.05, using GPower 3.1 software. The detailed outcomes of the power analysis are presented in Table 3. The power analysis graph illustrates the results of a two-tailed hypothesis test and assesses the likelihood of detecting an effect of a specified magnitude based on variables such as sample size, effect size, and significance level. Our findings indicate that the sample sizes from the selected studies were sufficient to meet this stringent significance level, hence ensuring the robustness and reliability of our conclusions. This thorough technique confirmed that our meta-analysis effectively identified significant relationships among the analysed SNPs, as illustrated in Figure 9.

Discussion

This meta-analysis assessed the relationship between a single gene and four specific genetic variations in 13,229 patients. Our comprehensive findings indicate that miR-146a, miR-499, and miR-196a2 were consistently correlated with CAD, while there was no association with miR-149a. Further analysis based on ethnicity revealed a significant correlation between miR-146a and miR-499 genetic variations and CAD risk in Asian populations.

The findings from our study are largely consistent with those of previous meta-analyses examining the miR-146a polymorphism. For example, Bastami et al. analyzed 30 studies involving 14,497 controls and 13,186 CAD patients but found no significant correlation between this variant and CAD risk.⁴¹ Similarly, Bao et al. reported no strong association in their meta-analysis of 18 studies (6,859 CAD cases and 8,469 controls).⁴² In contrast, a subsequent meta-analysis by Bao et al, including eight studies (3,097 controls and 3,138 cases), Similarly, Wang et al. performed a meta-analysis of eight studies with 3,468 CAD cases and

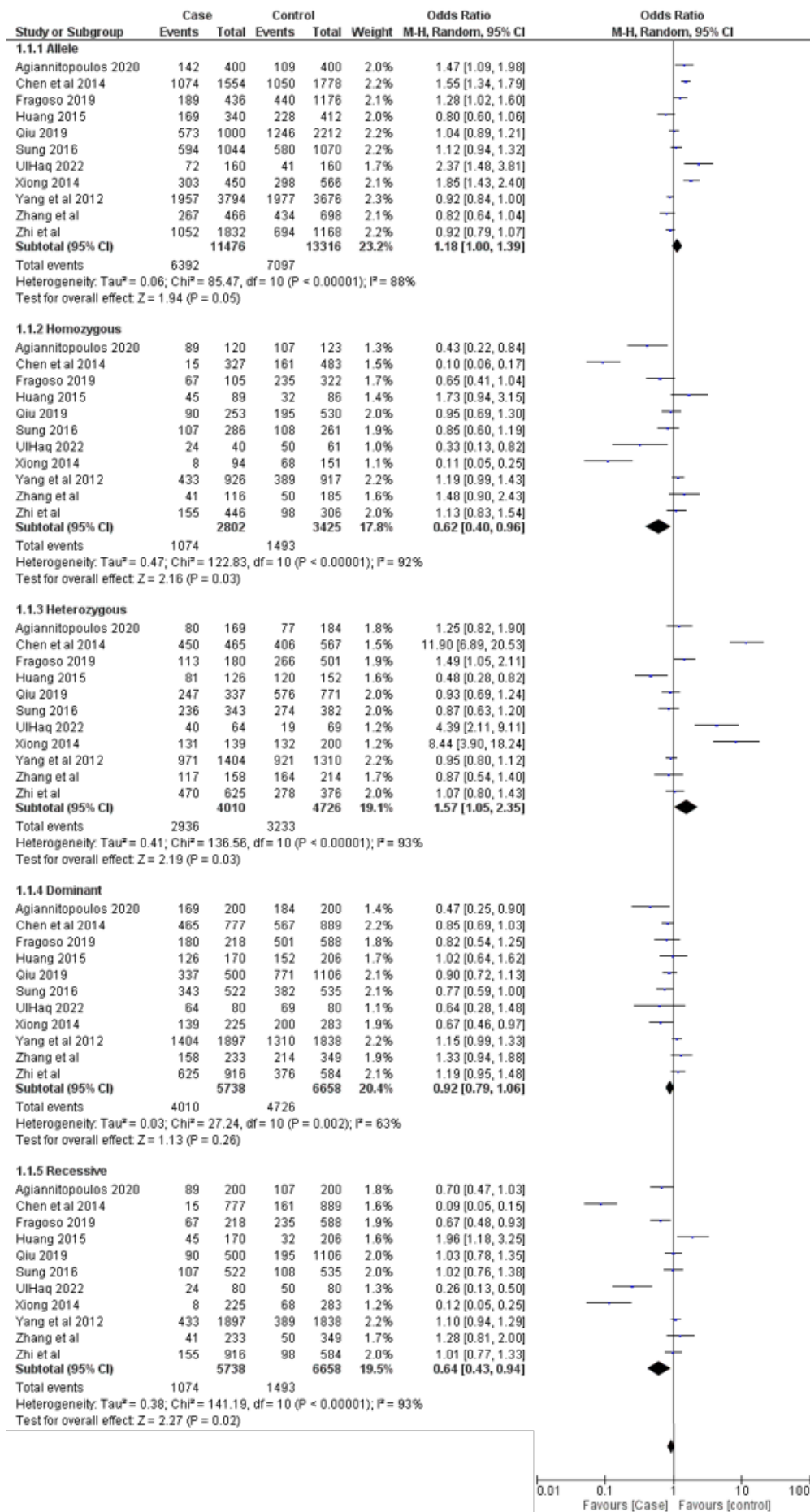


Figure 4. Forest plot showing an association between the miR-196a2 rs11614913 T>C gene polymorphism and CAD risk in the genetic models

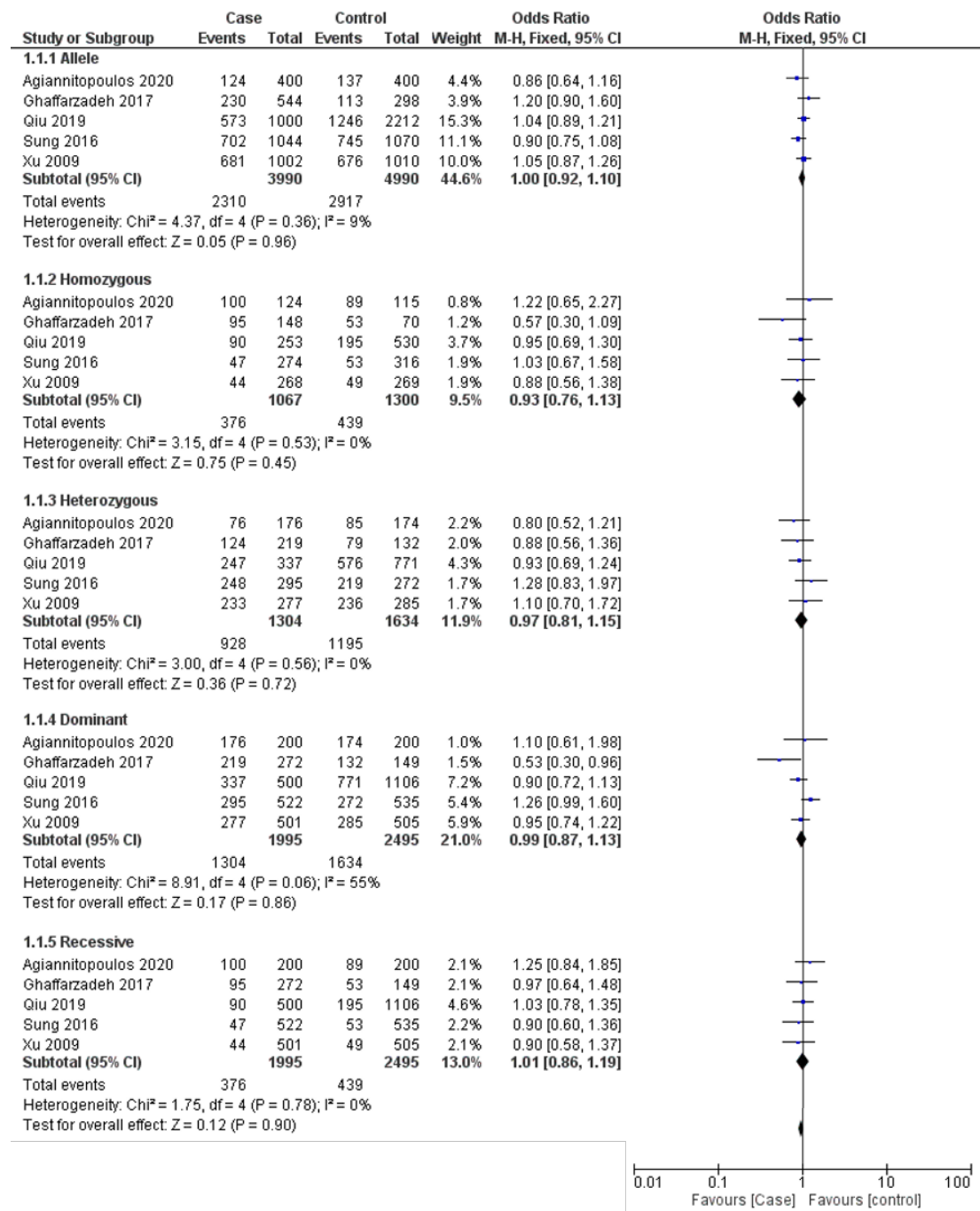


Figure 5. Forest plot showing an association between the miR-149a-rs2292832 gene polymorphism and CAD risk in the genetic models

3,425 controls and another by Zhou et al. with five studies (1,565 CAD patients and 1,541 controls) found significant associations, particularly among Asian populations, but not among Caucasians.^{43,44,45} In our analysis, we also identified a significant association between miR-146a and CAD risk, consistent with these ethnicity-dependent findings. However, we observed substantial heterogeneity across most genetic models ($I^2 > 50\%$), which warrants cautious interpretation. The observed heterogeneity may stem from differences in population genetic backgrounds, sample sizes, genotyping methods, and diagnostic criteria for CAD among the included studies. Additionally, environmental factors such as diet, smoking, and metabolic comorbidities may interact with genetic susceptibility, further amplifying

variability across studies. Furthermore, several models demonstrated wide confidence intervals and borderline significance, suggesting potential instability in the pooled effect estimates. These findings indicate that, although miR-146a may contribute to CAD susceptibility, the association should be viewed as suggestive rather than conclusive. Nonetheless, by incorporating newer studies and applying more rigorous quality assessments, our analysis provides an updated and more reliable pooled estimate supporting an ethnicity-dependent effect of the miR-146a polymorphism on CAD risk.

The findings regarding the miR-196a2 polymorphism revealed variable and model-dependent associations with CAD risk, rather than a uniformly consistent effect. Some

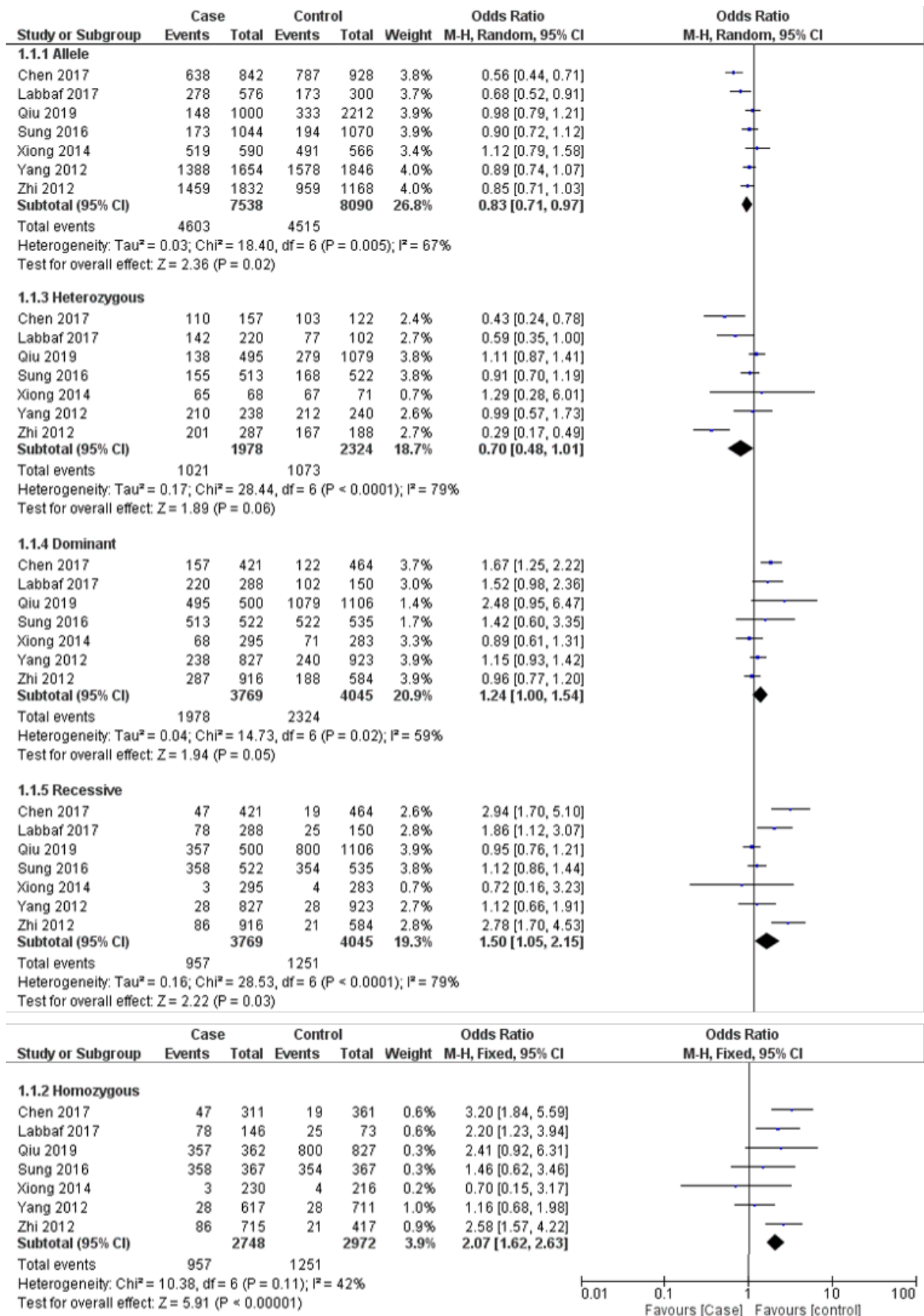


Figure 6. Forest plot showing an association between the miR-499 rs3746444 A>G gene polymorphism and CAD risk in the genetic models

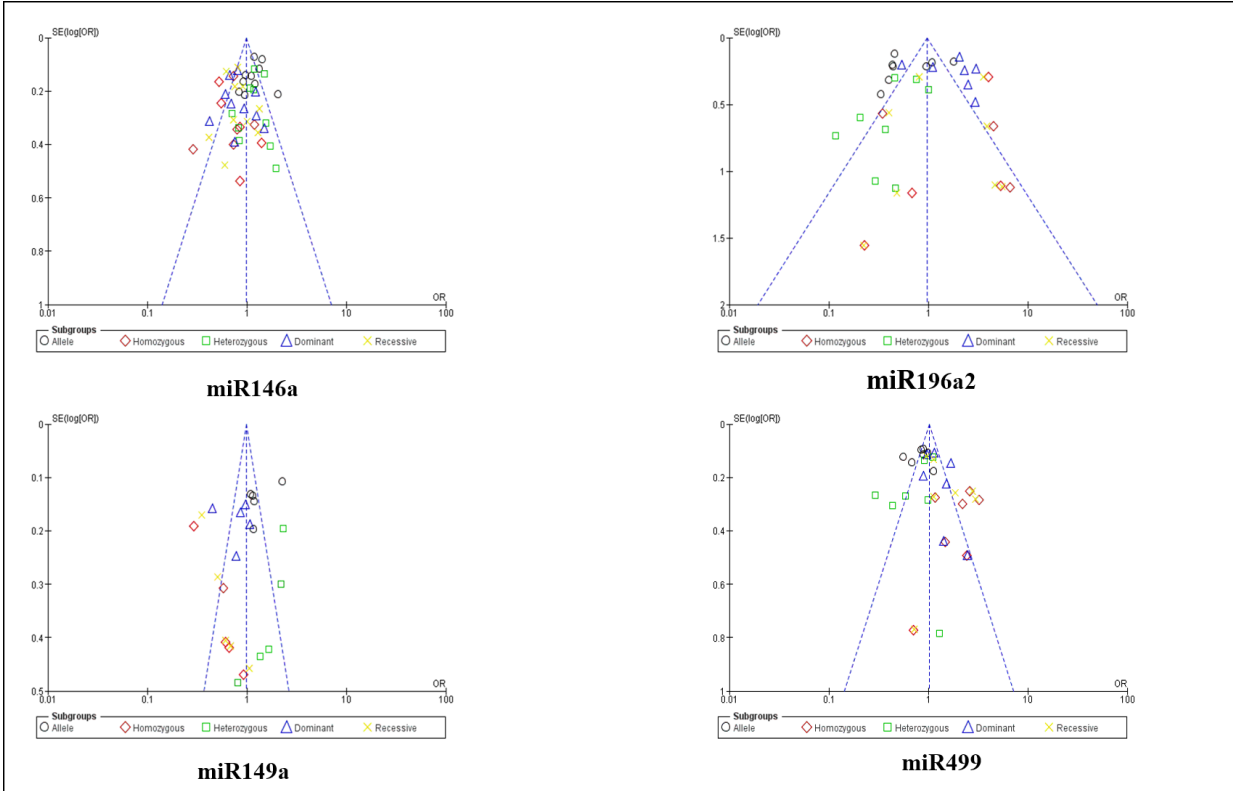


Figure 7. Funnel plots of publication biases on the relationships between miR-146a rs2910164, miR149a-rs2292832, miR-196a2 rs11614913, and miR-499 rs3746444 polymorphisms and CAD risk

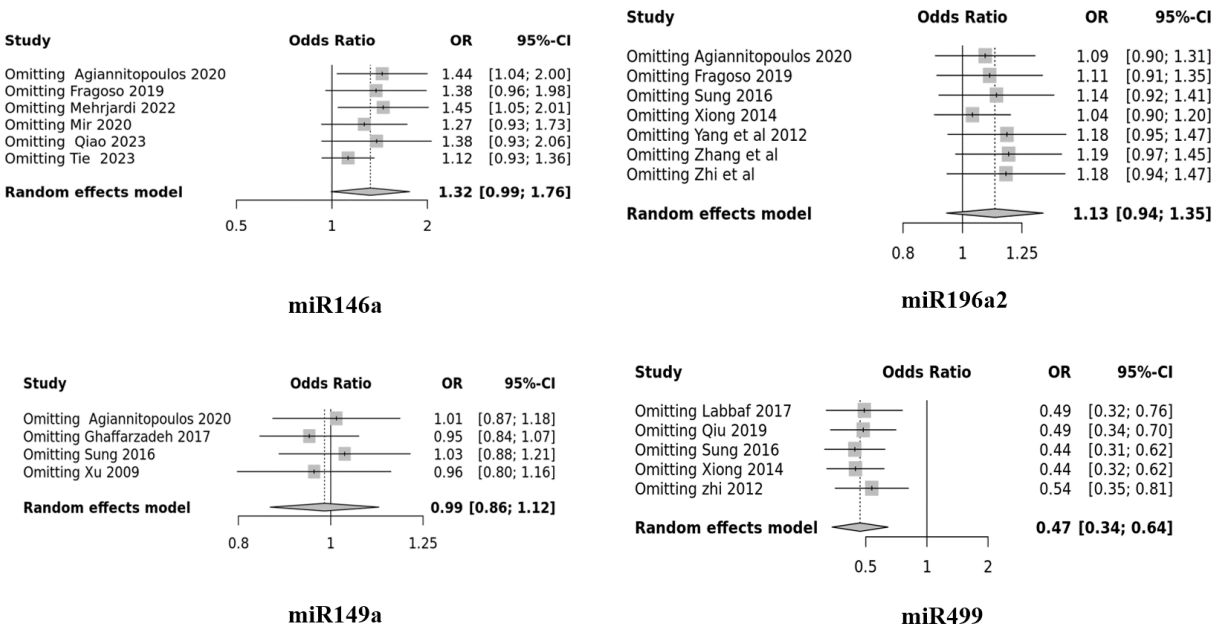


Figure 8. sensitivity analysis of genetic variants of miR-146a rs2910164, miR149a-rs2292832, miR-196a2 rs11614913, and miR-499 rs3746444 polymorphisms and CAD risk

genetic models, particularly the recessive and codominant models, demonstrated significant associations, whereas others showed weak or non-significant results. This pattern of inconsistency was especially evident across ethnic subgroups, with significant effects observed mainly in Asian populations, while no clear association emerged among Caucasians. These mixed outcomes are partly in line with the findings, for instance, Xie et

al. analyzed five studies including 3,676 patients with coronary heart disease and 3,397 controls, demonstrating a strong correlation under codominant, overdominant, and recessive models.⁴⁶ Similarly, Liu et al. evaluated seven studies comprising 6,146 CAD patients and 5,800 controls and found a significant association, particularly among Asian populations.⁴⁷ In contrast, Bastami et al. (2018)⁴¹ did not detect any relationship between miR-

196a2 polymorphism and CAD, possibly because of smaller sample sizes and lack of stratified analyses. In our meta-analysis, the pooled results confirmed a positive association between the miR-196a2 variant and CAD, which remained significant in Asian subgroups. However, we observed moderate heterogeneity across genetic models ($I^2 \approx 40\text{--}60\%$). This variability may reflect differences in ethnicity, study design, and genotyping approaches, as well as unmeasured environmental modifiers such as smoking and lipid profiles. While our broader inclusion of recent datasets improved statistical power, the confidence intervals for some genetic models were relatively wide, implying uncertainty in the precise magnitude of effect. Therefore, the association between miR-196a2 rs11614913 and CAD should be considered potentially meaningful but requiring confirmation through large, multicenter, population-based studies using standardized methodologies.

In contrast to the other variants examined, our analysis revealed no substantial correlation between the miR-149a polymorphism and CAD risk across any genetic model. This finding diverges from several earlier meta-analyses that reported weak or borderline associations between miR-149a and CAD. Differences in results may be attributed to

limited sample sizes, ethnic variation, and heterogeneity in study design and analytical methods across previous investigations. In particular, some earlier analyses included small or mixed cohorts without consistent adjustment for confounding factors, which may have inflated marginal associations.^{39,45} In our study, the inclusion of additional, higher-quality datasets and the use of stricter inclusion criteria likely improved the reliability of the pooled estimates, leading to a more conservative outcome. The lack of statistical significance observed here suggests that miR-149a may exert only a minor or population-specific influence on CAD susceptibility, or that its effect is mediated indirectly through interactions with other genetic or environmental factors. While this negative result adds clarity to an area of conflicting evidence, further large-scale studies in diverse populations are warranted to verify whether miR-149a contributes to CAD pathogenesis under specific conditions.

The results for miR-499 showed a robust association with CAD, in line with several previous meta-analyses. Lu et al. (2019) analyzed nine studies involving 4,603 controls and 5,063 CAD patients and demonstrated a significant relationship between this polymorphism and CAD risk.⁴⁸ Similarly, Xie et al. (2017)⁴⁶ and Liu et al. (2017)⁴⁷ reported consistent associations between miR-499 and CAD across multiple genetic models. These converging findings across independent analyses strongly support a role for miR-499 in the genetic susceptibility to CAD. The biological plausibility of this association is supported by evidence that miR-499 influences cardiac muscle gene regulation, apoptosis, and inflammatory signaling pathways, all of which are critical to atherosclerotic progression. Although some heterogeneity was observed, particularly among studies using distinct

Table 3. Power analysis for miR gene polymorphism and CAD

Gene	SNP	No of studies	Cases	Controls	A-error prob	Power (1- β error prob)
miR - 146a	rs2910164	9	1919	2111	0.05	0.9
miR - 196a2	rs11614913	11	5738	6658	0.05	1
miR - 149a	rs2292832	5	1995	2495	0.05	0.9
miR - 499	rs3746444	7	3769	4045	0.05	1

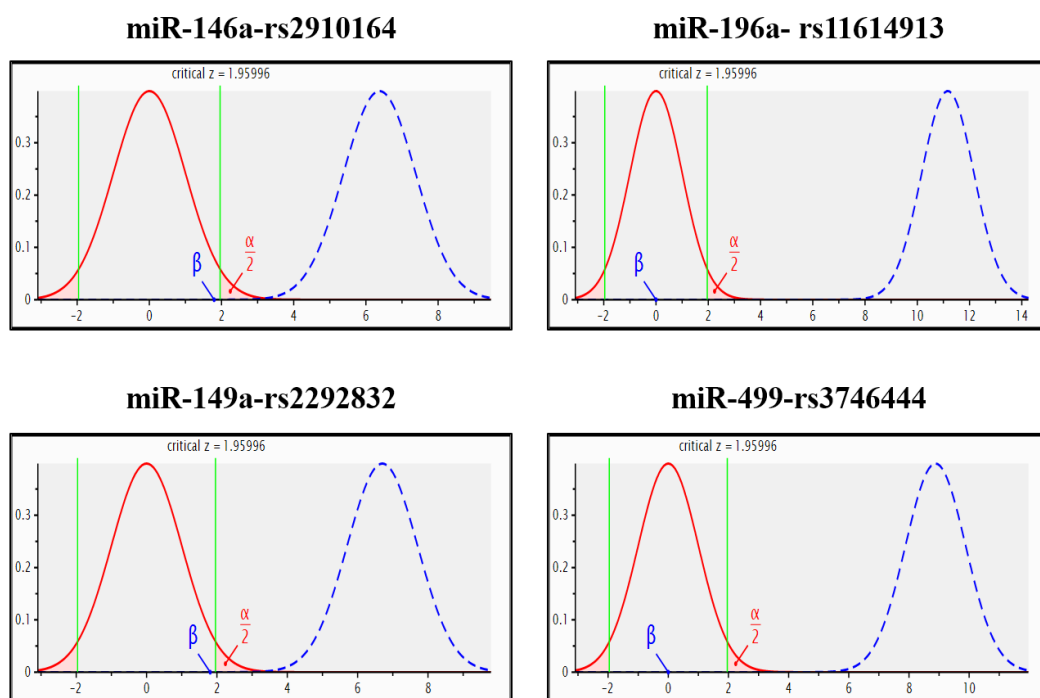


Figure 9. Power analysis for miR gene polymorphism and CAD

genotyping assays, the direction of association remained stable in sensitivity analyses, suggesting the results are statistically robust. Our meta-analysis, which incorporated a larger and more ethnically diverse dataset than most previous studies, provides updated confirmation that miR-499 rs3746444 is a significant genetic determinant of CAD risk.

The findings of our study showed substantial differences in the overall populations of miR-146a, miR-149, miR-196a2, and miR-499 across the five genetic models. We performed subgroup analyses utilising genotyping technologies to examine the origins of these variances and ethnicity, but determined that they did not account for the discrepancies. It is crucial to acknowledge that our investigation encompassed solely published literature, potentially introducing bias. Furthermore, we identified publication bias in the studies included, as our meta-analysis relied exclusively on published research. Our sensitivity analyses confirmed the robustness of our conclusions, since the outcomes persisted despite the exclusion of certain studies. The sample sizes for the miR-196a2 and miR-499 polymorphisms were significantly larger than those in other meta-analyses. Furthermore, we performed literature searches in electronic databases employing a highly sensitive methodology.

The implications of these discoveries are substantial in clinical practice. Genetic screening for polymorphisms in miR-146a, miR-149, miR-196a2, and miR-499 can improve risk valuation and individualized CAD management. By identifying individuals with genetic predispositions, physicians can tailor their assessments and treatment strategies to more effectively target specific risk factors.

This meta-analysis possesses several limitations that warrant consideration. Although the overall sample size was considerable, certain ethnic subgroups, particularly Caucasian populations, had relatively small sample sizes, thereby diminishing the statistical ability to identify meaningful relationships. Second, we observed considerable heterogeneity across several genetic models. This heterogeneity may arise from multiple sources, including differences in population genetic backgrounds, allele frequency distributions, variations in genotyping techniques, and inconsistencies in CAD diagnostic criteria among the included studies. Additionally, environmental and lifestyle factors such as diet, smoking, and comorbid conditions may interact with miRNA polymorphisms and contribute to variability between studies. Despite using random-effects models to account for between-study variation, these factors could still influence the pooled effect estimates.

Furthermore, CAD is a multifactorial disease influenced by both genetic and non-genetic determinants. Our meta-analysis relied on aggregated data, which prevented adjustment for traditional confounders such as age, sex, smoking, hypertension, diabetes, obesity, and dyslipidemia. These unmeasured covariates may modify the observed genetic associations and partially explain interstudy differences. As a result, the findings should be interpreted

with caution, and future individual participant data based meta-analyses are warranted to explore gene–environment and gene–gene interactions. Finally, our analysis was limited to English-language publications, which may have introduced publication bias and restricted inclusion of studies from underrepresented populations.

Conclusion

Our research indicates that genetic differences in miR-146a, miR-196a2, and miR-499 may elevate the risk of coronary artery disease (CAD). These variants may act as possible indicators for CAD, illustrating the complex interaction among various genes in its progression. Future research must prioritise rigorously designed studies that examine gene–environment and gene–gene interactions to validate these associations. Performing functional investigations is crucial to understand how these genetic variations affect CAD risk. Advancing research on diverse populations, incorporating genetic findings with supplementary biomarkers, and investigating personalised treatment strategies based on genetic profiles are essential for enhancing our understanding and management of CAD.

Acknowledgments

The authors thank the Chettinad Academy of Research and Education for their constant support and encouragement.

Authors' Contribution

Conceptualization: Ramakrishnan Veerabathiran
Formal Analysis: Praveen Kumar Chandra Sekar
Methodology: Praveen Kumar Chandra Sekar
Project Administration: Ramakrishnan Veerabathiran
Software: Praveen Kumar Chandra Sekar
Supervision: Ramakrishnan Veerabathiran
Validation: Praveen Kumar Chandra Sekar, Ramakrishnan Veerabathiran
Writing–Original Draft: Praveen Kumar Chandra Sekar
Writing–Review & Editing: Praveen Kumar Chandra Sekar, Ramakrishnan Veerabathiran

Competing Interests

The authors declare no conflict of interest to report

Ethical Approval

Not applicable.

Funding

Not applicable.

Supplementary Files

Supplementary file contain Table S1.

Reference

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020;396(10258):1204–22. doi:10.1016/s0140-6736(20)30925-9
2. Shao C, Wang J, Tian J, Tang YD. Coronary artery disease: from mechanism to clinical practice. *Adv Exp Med Biol* 2020;1177:1–36. doi:10.1007/978-981-15-2517-9_1
3. Sudhan M, Janakiraman V, Ahmad SF, Attia SM, Subramanian R, Devi D, et al. A comprehensive insight from molecular docking and dynamics with clinical investigation on the impact of direct oral anticoagulants on atheroprotective protein

- in atrial fibrillation. *BMC Pharmacol Toxicol* 2024;25(1):56. doi:[10.1186/s40360-024-00785-z](https://doi.org/10.1186/s40360-024-00785-z)
4. Yang L, Zheng B, Gong Y. Global, regional and national burden of ischemic heart disease and its attributable risk factors from 1990 to 2021: a systematic analysis of the Global Burden of Disease Study 2021. *BMC Cardiovasc Disord* 2025;25(1):625. doi:[10.1186/s12872-025-05022-x](https://doi.org/10.1186/s12872-025-05022-x)
 5. Sobha SP, Kesavarao KE. Prognostic effect of GSTM1/GSTT1 polymorphism in determining cardiovascular diseases risk among type 2 diabetes patients in South Indian population. *Mol Biol Rep* 2023;50(8):6415-23. doi:[10.1007/s11033-023-08514-1](https://doi.org/10.1007/s11033-023-08514-1)
 6. Chandra Sekar PK, Govindaraj A, Veerabathiran R. Genetic variants of APOE and CCR4 as determinants of myocardial infarction among type 2 diabetes patients: a South Indian case-control analysis. *Mol Biol Rep* 2026;53(1):326. doi:[10.1007/s11033-026-11489-4](https://doi.org/10.1007/s11033-026-11489-4)
 7. Lerman JB, Parness IA, Shenoy RU. Body weights in adults with congenital heart disease and the obesity frequency. *Am J Cardiol* 2017;119(4):638-42. doi:[10.1016/j.amjcard.2016.10.050](https://doi.org/10.1016/j.amjcard.2016.10.050)
 8. Pourkeramati A, Zare Mehrjardi E, Dehghan Tezerjani M, Seifati SM. Association of GSTP1, GSTT1 and GSTM1 gene variants with coronary artery disease in Iranian population: a case-control study. *Int J Gen Med* 2020;13:249-59. doi:[10.2147/ijgm.S252552](https://doi.org/10.2147/ijgm.S252552)
 9. Nikpay M, Goel A, Won HH, Hall LM, Willenborg C, Kanoni S, et al. A comprehensive 1,000 Genomes-based genome-wide association meta-analysis of coronary artery disease. *Nat Genet* 2015;47(10):1121-30. doi:[10.1038/ng.3396](https://doi.org/10.1038/ng.3396)
 10. Deloukas P, Kanoni S, Willenborg C, Farrall M, Assimes TL, Thompson JR, et al. Large-scale association analysis identifies new risk loci for coronary artery disease. *Nat Genet* 2013;45(1):25-33. doi:[10.1038/ng.2480](https://doi.org/10.1038/ng.2480)
 11. Sitingjak BD, Murdaya N, Rachman TA, Zakiah N, Barliana MI. The potential of single nucleotide polymorphisms (SNPs) as biomarkers and their association with the increased risk of coronary heart disease: a systematic review. *Vasc Health Risk Manag* 2023;19:289-301. doi:[10.2147/vhrm.S405039](https://doi.org/10.2147/vhrm.S405039)
 12. Yang Y, Yu T, Jiang S, Zhang Y, Li M, Tang N, et al. miRNAs as potential therapeutic targets and diagnostic biomarkers for cardiovascular disease with a particular focus on WO2010091204. *Expert Opin Ther Pat* 2017;27(9):1021-9. doi:[10.1080/13543776.2017.1344217](https://doi.org/10.1080/13543776.2017.1344217)
 13. Li G, Liu B, Jiang Q, Zhang J, Xin S, Xu K. The association of two common polymorphisms in miRNAs with diabetes mellitus: a meta-analysis. *Medicine (Baltimore)* 2019;98(40): e17414. doi:[10.1097/md.00000000000017414](https://doi.org/10.1097/md.00000000000017414)
 14. Kondracki B, Kłoda M, Jusiak-Kłoda A, Kondracka A, Waciński J, Waciński P. microRNA expression in patients with coronary artery disease and hypertension-a systematic review. *Int J Mol Sci* 2024;25(12):6430. doi:[10.3390/ijms25126430](https://doi.org/10.3390/ijms25126430)
 15. Lee S. Cardiovascular disease and miRNAs: possible oxidative stress-regulating roles of miRNAs. *Antioxidants (Basel)* 2024;13(6):656. doi:[10.3390/antiox13060656](https://doi.org/10.3390/antiox13060656)
 16. Manikandan M, Munirajan AK. Single nucleotide polymorphisms in microRNA binding sites of oncogenes: implications in cancer and pharmacogenomics. *OMICS* 2014;18(2):142-54. doi:[10.1089/omi.2013.0098](https://doi.org/10.1089/omi.2013.0098)
 17. Xue S, Zhu W, Liu D, Su Z, Zhang L, Chang Q, et al. Circulating miR-26a-1, miR-146a and miR-199a-1 are potential candidate biomarkers for acute myocardial infarction. *Mol Med* 2019;25(1):18. doi:[10.1186/s10020-019-0086-1](https://doi.org/10.1186/s10020-019-0086-1)
 18. Wang Y, Wang X, Li Z, Chen L, Zhou L, Li C, et al. Two single nucleotide polymorphisms (rs2431697 and rs2910164) of miR-146a are associated with risk of coronary artery disease. *Int J Environ Res Public Health* 2017;14(5):514. doi:[10.3390/ijerph14050514](https://doi.org/10.3390/ijerph14050514)
 19. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. In: 3rd Symposium on Systematic Reviews: Beyond the Basics. Oxford, UK: St Catherine's College; 2000.
 20. Fragoso JM, Ramírez-Bello J, Martínez-Ríos MA, Peña-Duque MA, Posadas-Sánchez R, Delgadillo-Rodríguez H, et al. miR-196a2 (rs11614913) polymorphism is associated with coronary artery disease, but not with in-stent coronary restenosis. *Inflamm Res* 2019;68(3):215-21. doi:[10.1007/s00011-018-1206-z](https://doi.org/10.1007/s00011-018-1206-z)
 21. Bastami M, Ghaderian SM, Omrani MD, Mirfakhraie R, Vakili H, Alipour Parsa S, et al. miRNA-related polymorphisms in miR-146a and TCF21 are associated with increased susceptibility to coronary artery disease in an Iranian population. *Genet Test Mol Biomarkers* 2016;20(5):241-8. doi:[10.1089/gtmb.2015.0253](https://doi.org/10.1089/gtmb.2015.0253)
 22. Tie J, Takanari H, Ota K, Okuda T. Role of miR-143 and miR-146 in risk evaluation of coronary artery diseases in autopsied samples. *Genes (Basel)* 2023;14(2):471. doi:[10.3390/genes14020471](https://doi.org/10.3390/genes14020471)
 23. Ali HM, Ellakwa DE, Elaraby NM, Zaher AM, Amr KS. Study the association of microRNA polymorphisms (miR-146a, miR-4513) with the risk of coronary heart diseases in Egyptian population. *J Biochem Mol Toxicol* 2023;37(3): e23284. doi:[10.1002/jbt.23284](https://doi.org/10.1002/jbt.23284)
 24. Qiao XR, Zheng T, Xie Y, Yao X, Yuan Z, Wu Y, et al. miR-146a rs2910164 (G/C) polymorphism is associated with the development and prognosis of acute coronary syndromes: an observational study including case control and validation cohort. *J Transl Med* 2023;21(1):325. doi:[10.1186/s12967-023-04140-4](https://doi.org/10.1186/s12967-023-04140-4)
 25. Agiannitopoulos K, Samara P, Papadopoulou M, Efthymiadou A, Papadopoulou E, Tsaousis GN, et al. miRNA polymorphisms and risk of premature coronary artery disease. *Hellenic J Cardiol* 2021;62(4):278-84. doi:[10.1016/j.hjc.2020.01.005](https://doi.org/10.1016/j.hjc.2020.01.005)
 26. Mir R, Elfaki I, Jha C, Javid J, Rehman S, Banu S, et al. Molecular evaluation of microRNA-146 gene variability (rs2910164 C>G) and its association with increased susceptibility to coronary artery disease. *Microna* 2020;9(5):363-72. doi:[10.2174/2211536609666201209151130](https://doi.org/10.2174/2211536609666201209151130)
 27. Chen C, Hong H, Chen L, Shi X, Chen Y, Weng Q. Association of microRNA polymorphisms with the risk of myocardial infarction in a Chinese population. *Tohoku J Exp Med* 2014;233(2):89-94. doi:[10.1620/tjem.233.89](https://doi.org/10.1620/tjem.233.89)
 28. Huang S, Lv Z, Deng Q, Li L, Yang B, Feng J, et al. A genetic variant in pre-miR-146a (rs2910164 C>G) is associated with the decreased risk of acute coronary syndrome in a Chinese population. *Tohoku J Exp Med* 2015;237(3):227-33. doi:[10.1620/tjem.237.227](https://doi.org/10.1620/tjem.237.227)
 29. Qiu H, Chen Z, Lv L, Tang W, Hu R. Associations between microRNA polymorphisms and development of coronary artery disease: a case-control study. *DNA Cell Biol* 2020;39(1):25-36. doi:[10.1089/dna.2019.4963](https://doi.org/10.1089/dna.2019.4963)
 30. Sung JH, Kim SH, Yang WI, Kim WJ, Moon JY, Kim JJ, et al. miRNA polymorphisms (miR-146a, miR-149, miR-196a2 and miR-499) are associated with the risk of coronary artery disease. *Mol Med Rep* 2016;14(3):2328-42. doi:[10.3892/mmr.2016.5495](https://doi.org/10.3892/mmr.2016.5495)
 31. Haq TU, Zahoor A, Ali Y, Chen Y, Jalil F, Shah AA. Genetic variants of miR27A, miR196A2 may impact the risk for the onset of coronary artery disease in the Pakistani population. *Genes (Basel)* 2022;13(5):747. doi:[10.3390/genes13050747](https://doi.org/10.3390/genes13050747)
 32. Xiong XD, Cho M, Cai XP, Cheng J, Jing X, Cen JM, et al. A common variant in pre-miR-146 is associated with coronary artery disease risk and its mature miRNA expression. *Mutat Res* 2014;761:15-20. doi:[10.1016/j.mrfmmm.2014.01.001](https://doi.org/10.1016/j.mrfmmm.2014.01.001)
 33. Yang Y. Association Between Pre-miRNA Genetic Polymorphism and Coronary Heart Disease and a Prospective Study of the Combined Effects of Total Cholesterol and High Blood Pressure on Fatal Cardiovascular Disease in a Male Shougang Group [dissertation]. Beijing Union Medical College; 2012.
 34. Yu ZH, Lina WA, Hong ZH, Weihong TA, Jiaju ZH, Yi ZH, et

- al. Genetic susceptibility association study on polymorphisms of miRNAs genes and the risk of premature coronary artery disease. *J Clin Cardiol* 2013;29(1):21-5. doi:[10.13201/j.issn.1001-1439.2013.01.019](https://doi.org/10.13201/j.issn.1001-1439.2013.01.019)
35. Zhi H, Wang L, Ma G, Ye X, Yu X, Zhu Y, et al. Polymorphisms of miRNAs genes are associated with the risk and prognosis of coronary artery disease. *Clin Res Cardiol* 2012;101(4):289-96. doi:[10.1007/s00392-011-0391-3](https://doi.org/10.1007/s00392-011-0391-3)
36. Ghaffarzadeh M, Ghaedi H, Alipoor B, Omrani MD, Kazerouni F, Shanaki M, et al. Association of miR-149 (RS2292832) variant with the risk of coronary artery disease. *J Med Biochem* 2017;36(3):251-8. doi:[10.1515/jomb-2017-0005](https://doi.org/10.1515/jomb-2017-0005)
37. Xu J, Hu Z, Xu Z, Gu H, Yi L, Cao H, et al. Functional variant in microRNA-196a2 contributes to the susceptibility of congenital heart disease in a Chinese population. *Hum Mutat* 2009;30(8):1231-6. doi:[10.1002/humu.21044](https://doi.org/10.1002/humu.21044)
38. Yang Y. Common Genetic Variations in Pre-miRNAs and the Risk of Coronary Heart Disease in a Chinese Han Population [dissertation]. Beijing: Peking Union Medical College; 2012.
39. Labbaf A, Ghaedi H, Alipoor B, Omrani MD, Kazerouni F, Shanaki M, et al. The pre-miR-499 variant rs3746444 may contribute to coronary artery disease susceptibility: a case-control and meta-analysis study. *Clin Lab* 2017;63(3):587-95. doi:[10.7754/Clin.Lab.2016.161011](https://doi.org/10.7754/Clin.Lab.2016.161011)
40. Chen W, Shao D, Gu H, Gong J, Zhang J. Hsa-miR-499 rs3746444 T/C polymorphism is associated with increased risk of coronary artery disease in a Chinese population. *Acta Cardiol Sin* 2017;33(1):34-40. doi:[10.6515/acs20160303a](https://doi.org/10.6515/acs20160303a)
41. Bastami M, Choupani J, Saadatian Z, Zununi Vahed S, Mansoori Y, Daraei A, et al. miRNA polymorphisms and risk of cardio-cerebrovascular diseases: a systematic review and meta-analysis. *Int J Mol Sci* 2019;20(2):293. doi:[10.3390/ijms20020293](https://doi.org/10.3390/ijms20020293)
42. Bao Q, Li R, Wang C, Wang S, Cheng M, Pu C, et al. Association between microRNA-146a rs2910164 polymorphism and coronary heart disease: an updated meta-analysis. *Medicine (Baltimore)* 2022;101(46): e31860. doi:[10.1097/md.00000000000031860](https://doi.org/10.1097/md.00000000000031860)
43. Bao MH, Xiao Y, Zhang QS, Luo HQ, Luo J, Zhao J, et al. Meta-analysis of miR-146a polymorphisms association with coronary artery diseases and ischemic stroke. *Int J Mol Sci* 2015;16(7):14305-17. doi:[10.3390/ijms160714305](https://doi.org/10.3390/ijms160714305)
44. Wang Y, Li Q, Mambiya M, Zhang K, Yang L, Zhang Q, et al. A meta-analysis of the association between microRNA-196a2 and risk of ischemic stroke and coronary artery disease in Asian population. *J Stroke Cerebrovasc Dis* 2018;27(11):3008-19. doi:[10.1016/j.jstrokecerebrovasdis.2018.06.035](https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.06.035)
45. Zhou HY, Wei Q, Shi XD, Cao HY, Qin L. miR-146a rs2910164 polymorphism might be associated with coronary artery disease risk in Asians. *Cell Mol Biol (Noisy-le-grand)* 2017;63(8):27-9. doi:[10.14715/cmb/2017.63.8.6](https://doi.org/10.14715/cmb/2017.63.8.6)
46. Xie X, Shi X, Xun X, Rao L. Association between microRNA polymorphisms and coronary heart disease: a meta-analysis. *Herz* 2017;42(6):593-603. doi:[10.1007/s00059-016-4495-4](https://doi.org/10.1007/s00059-016-4495-4)
47. Liu X, You L, Zhou R, Zhang J. Significant association between functional microRNA polymorphisms and coronary heart disease susceptibility: a comprehensive meta-analysis involving 16484 subjects. *Oncotarget* 2017;8(4):5692-702. doi:[10.18632/oncotarget.14249](https://doi.org/10.18632/oncotarget.14249)
48. Lu JY, Chen MH, Zhang JF, Li ZZ, Liao PH. Association between miR-499 rs3746444 polymorphism and coronary heart disease susceptibility: an evidence-based meta-analysis of 5063 cases and 4603 controls. *Gene* 2019;698:34-40. doi:[10.1016/j.gene.2019.02.045](https://doi.org/10.1016/j.gene.2019.02.045)