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Association of cardiovascular disease and urate levels with aortic aneurysm: a bilateral mendelian randomization study

Yuanyuan Xiao[1] & Tao Xiang[1,2]✉

The aim of this study is to investigate the potential causal relationships between coronary artery disease (CAD), myocardial infarction (MI), urate levels, and aortic aneurysm (AA), abdominal aortic aneurysm (AAA), thoracic aortic aneurysm(TAA), aortic dissection (AD) in individuals of European ancestry. To examine the potential causal relationships between CAD, MI, and urate levels with AA, AAA, TAA, AD, respectively, we performed a two-sample Mendelian randomization (MR) analysis. Genetic instruments that reached genome-wide significance ($p < 5 \times 10 - 8$) for risk factors were obtained from genome-wide association studies(GWASs) conducted on individuals of European origin. On the other hand, genetic instruments of AA, AAA, TAA or AD were chosen from the FinnGen cohort. The primary analysis employed the inverse-variance weighted MR method, while sensitivity analyses were conducted using MR-Egger, weighted median MR, MR pleiotropy residual sum and outlier, and Phenoscanner searching. In addition, we performed the MR-Egger intercept analysis to identify potential pleiotropy and utilized Cochran's Q statistics to evaluate heterogeneity. Additionally, we conducted bidirectional Mendelian randomization experiments to mitigate the potential influence of reverse causation. According to the results of our study, there were statistically significant higher risks for AA in relation to CAD/MI(odds ratio (OR) with 95% confidence interval (CI): 1.309 (1.150–1.490), and 1.255 (1.147–1.373). Similarly, there were statistically significant higher risks for AAA in relation to CAD and MI (OR with 95% CI: 1.383 (1.189–1.609), and 1.352 (1.178–1.552). The sensitivity analysis demonstrated that the causative effects of CAD/MI, and AA /AAA, were robust. A positive causal link was observed between CAD/MI, and AA/AAA. Nevertheless, no causal link was found between CAD, MI, urate levels, and TAA .

AA is the second most prevalent aortic disorder behind atherosclerosis, including AAA and TAA. It poses a significant risk of abrupt mortality and is defined by localized, gradual, and irreversible expansion of the aorta's whole thickness[1]. The progression of AA is characterized by a sluggish rate, and the presence of big aneurysms can potentially result in aortic rupture, leading to an abrupt fatality[2]. Recent research indicates a substantial occurrence of AA in individuals diagnosed with coronary disease[3,4]. Research has also demonstrated a positive correlation between the severity of CAD and the prevalence of AA[5]. According to a meta-analysis, several risk variables have been identified for AA, including diabetes mellitus, smoking habits, hypertension, and CAD[6]. However, a study conducted by researchers discovered a potential negative correlation between CAD and AA development[7]. The potential causal relationship between AAA and atherosclerosis remains uncertain, as individuals with AAA often exhibit coexisting atherosclerotic conditions such as CAD. It is unclear if this observed association between AAA and atherosclerosis is attributable to shared risk factors or if there exists a direct causal link. In addition to the aforementioned commonly recognized risk factors, it has been observed in certain investigations that there exists an association between urate levels and AA[8]. Hence, further investigation is required to establish the causal association between CAD, levels of urate, and AA.

The field of observational epidemiology has encountered numerous obstacles in its pursuit of identifying the etiology of diseases and establishing causal relationships. MR is a reliable tool for determining how an exposure affects an outcome causally[9–11]. The analytical approach is characterized by a reduced vulnerability to bias caused by confounding variables and effectively avoids potential bias resulting from reverse causation. This is achieved by employing genetic variants, often single-nucleotide polymorphisms (SNPs), that are randomly assigned after

[1]Department of Emergency, The Third People's Hospital of Chengdu, Chengdu, Sichuan, China. [2]Present address: No. 68, Qinglong Street, Qingyang District, Chengdu, Sichuan, China. ✉email: xt1142752929@126.com

conception as instrumental variables (IVs) for exposure[11–13]. To ensure unbiased outcomes, three assumptions of MR need to be satisfied: (a) the genetic IVs must exhibit a robust association with the exposure under investigation; (b) the genetic IVs should not be correlated with any confounding factors that are associated with both the chosen exposure and the outcome; and (c) the genetic IVs should exclusively influence the outcome through the exposures being studied, without any involvement of alternative biological pathways[14]. In this study, a two-sample MR analysis was used to assess the causative relationship between CAD, MI, urate levels, and AA, AAA, TAA or AD. Additionally, a reverse MR analysis was performed to examine the reciprocal causal relationship between AA and CAD.

Methods

The sources of data

The analysis used publicly available summary statistics from GWASs, especially concentrating on the features of European people (refer to Table 1). The summary statistics for CAD[15] with a sample size of 296,525 and MI[16] with a sample size of 461,823 were acquired from the UK Biobank study. Additionally, the summary statistics for urate[17] with a sample size of 110,347 were collected from the Global Urate Genetics Consortium (GUGC). The analysis involved the examination of SNPs linked to AA, AAA, TAA and AD using data obtained from the FinnGen R9 release. The sample size for AA was 356,934, while for AD it was 350,420. The datasets included in this investigation are accessible through publicly available databases and were granted ethical approval prior to their utilization. Consequently, the present investigation did not necessitate any supplementary ethical clearance. The detailed descriptive information for these IVs is showed in Supplementary Table 1(S1).

The choice of the genetic tools

Initially, we identified distinct SNPs that exhibited a robust association with CAD, MI, and urate levels, respectively, as shown by p-values below 5×10^{-8}. Additionally, in order to exclude SNPs that exhibited significant linkage disequilibrium (LD), we conducted the clumping technique with a threshold of $R2<0.001$ and a window size of 10,000 kilobases[18]. Furthermore, SNPs exhibiting a minor allele frequency (MAF) below 0.01 were also excluded. In order to ensure that the impact alleles are consistent within the same allele, we conducted a process of harmonization on the exposure and outcome datasets. This involved removing SNPs with ambiguous alleles that did not align with each other, as well as SNPs with intermediate allele frequencies. Additionally, the F statistics were computed for each SNP both individually and collectively using the following formula: $F=R2(N-2)/(1 - R2)$. The symbol R2 is used to represent the variance of exposure that is accounted for by each independent variable. IVs that exhibited F statistics below ten were deemed to be weak instruments and were consequently eliminated from the analysis[19].

Statistical analysis

In this research, a variety of complimentary methodologies were employed to evaluate the causal effects of exposures on outcomes. These methodologies included the inverse variance weighted (IVW), the MR-Egger regression, the weighted mode and the weighted median methods. The IVW method was employed as the primary analytical approach. The IVW technique was predominantly utilized for estimating fundamental causal effects, aiming to yield the most accurate outcomes under the assumption that all chosen SNPs are legitimate IVs[20]. If the condition of all included SNPs being suitable IVs is satisfied, the IVW method yields a precise estimation[21]. The extra analysis methods employed in this study were MR-Egger, weighted median and the weighted mode. The MR-Egger regression approach has the capability to identify and account for pleiotropy, although its estimation accuracy is somewhat limited[22]. The weighted median provides a precise estimation under the condition that a minimum of 50% of IVs are valid[23].The weighted mode method is a method used to merge multiple Mendelian randomized estimation results. $P<0.05/(3*4)$.was considered as statistical significance after Bonferroni adjustment for multiple comparisons.

Pleiotropy and sensitivity analysis

The MR-Egger regression was employed in order to assess the potential presence of horizontal pleiotropy. The intercept term of the MR-Egger regression[24] provides an indication of the average pleiotropic influence of the IVs. The weighted mode method can reduce errors caused by deviations in the estimation results of certain

Trait	Year	Consortium	Population	Sample size	*n* Case	*n* Control
CAD	2017	UK Biobank	European	296,525	34,541	261,984
MI	2021	UK Biobank	European	461,823	20,917	440,906
Urate levels	2012	GUGC	European	110,347		
AA	2021	FinnGen	European	356,934	7395	349,539
AAA	2021	FinnGen	European	353,087	3548	349,539
TAA	2021	FinnGen	European	353,049	3510	349,539
AD	2021	FinnGen	European	350,420	881	349,539

Table 1. Baseline characteristics of coronary artery disease (CAD), myocardial infarction (MI), urate levels, aortic aneurysm (AA), abdominal aortic aneurysm (AAA), thoracic aortic aneurysm(TAA), and aortic dissection(AD) datasets.

genetic variations[25]. The presence of asymmetry in the funnel plot can also be seen as an indication of horizontal pleiotropy[10]. The MR-PRESSO test was performed to assess the presence of pleiotropy[26]. The functions of this method encompass the identification of horizontal pleiotropy, the adjustment for horizontal pleiotropy through the removal of outliers. To assess heterogeneity, we utilized the IVW method and MR-Egger regression. The degree of heterogeneity was measured using Cochran's Q statistic. Furthermore, we employed a leave-one-out analysis to assess the robustness and consistency of the findings. The analyses were conducted using the "TwoSampleMR"[10] and "MRPRESSO" packages in R version 4.2.3.

Results

Mendelian randomization analysis

The Fig. 1 displays the MR estimations for several approaches. Firstly, the IVW analysis revealed associations between CAD ($p=4.29E-05$, OR = 1.309), MI ($p=7.60E-07$, OR = 1.255), and urate levels ($p=0.039$, OR = 1.178) with AA, indicating a positive causal relationship (Fig. 1). The results of the weighted median and MR Egger analyses also indicated a statistically significant positive causal relationship between CAD, MI with AA ($p<0.004$, odds ratio > 1) (see Fig. 1). Nevertheless, the application of reverse Mendelian analysis does not

outcome	exposure	nsnp	method	OR (95% CI)	pval
AA	CAD	137	Inverse variance weighted	1.309 (1.150 to 1.490)	4.3e-05
		137	MR Egger	1.647 (1.257 to 2.158)	4.2e-04
		137	Weighted median	1.446 (1.123 to 1.862)	5.0e-03
	MI	72	Inverse variance weighted	1.255 (1.147 to 1.373)	7.6e-07
		72	MR Egger	1.394 (1.137 to 1.709)	2.1e-03
		72	Weighted median	1.414 (1.227 to 1.630)	9.1e-06
	Urate levels	24	Inverse variance weighted	1.178 (1.008 to 1.377)	3.9e-02
		24	MR Egger	1.070 (0.855 to 1.400)	5.6e-01
		24	Weighted median	1.119 (0.941 to 1.330)	2.1e-01
AAA	CAD	141	Inverse variance weighted	1.383 (1.189 to 1.609)	2.7e-05
		141	MR Egger	2.056 (1.470 to 2.876)	4.5e-05
		141	Weighted median	2.001 (1.302 to 3.077)	1.9e-03
	MI	73	Inverse variance weighted	1.352 (1.178 to 1.552)	1.8e-05
		73	MR Egger	1.404 (1.007 to 1.960)	4.9e-02
		73	Weighted median	1.189 (0.856 to 1.650)	3.0e-01
TAA	CAD	139	Inverse variance weighted	1.047 (0.932 to 1.178)	4.4e-01
		139	MR Egger	1.101 (0.858 to 1.412)	4.5e-01
		139	Weighted median	0.970 (0.796 to 1.182)	7.6e-01
	MI	69	Inverse variance weighted	1.101 (0.997 to 1.216)	5.8e-02
		69	MR Egger	0.979 (0.783 to 1.226)	8.6e-01
		69	Weighted median	0.995 (0.856 to 1.156)	9.5e-01
AD	CAD	142	Inverse variance weighted	1.098 (0.893 to 1.351)	3.8e-01
		142	MR Egger	1.377 (0.888 to 2.137)	1.5e-01
		142	Weighted median	1.297 (0.882 to 1.908)	1.9e-01
	MI	73	Inverse variance weighted	1.130 (0.938 to 1.360)	2.0e-01
		73	MR Egger	1.290 (0.846 to 1.967)	2.4e-01
		73	Weighted median	1.184 (0.844 to 1.662)	3.3e-01
CAD	AA	2	Inverse variance weighted	1.026 (0.897 to 1.174)	7.1e-01
MI	AA	2	Inverse variance weighted	0.995 (0.921 to 1.076)	9.0e-01

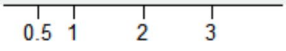

Fig. 1. Displays the estimated causal effects among CAD, MI, urate levels, and AA, as well as CAD, MI, and AAA, TAA, AD, utilizing various Mendelian randomization (MR) techniques.

reveal any causal association between AA and CAD/MI(Fig. 1). Secondly, the IVW analysis revealed significant associations between CAD ($p = 2.67E-05$, OR = 1.383) and MI ($p = 1.82E-05$, OR = 1.352)with AAA, indicating a positive causal relationship (Fig. 1). The heatmap shows the association between CAD/MI, urate levels and AA/AAA/TAA(Fig. 2). Additionally, the IVW conducted in this study revealed no significant causal relationships between genetically predicted CAD, MI, urate levels and TAA or AD, respectively(Fig. 1, Supplementary Table 2).

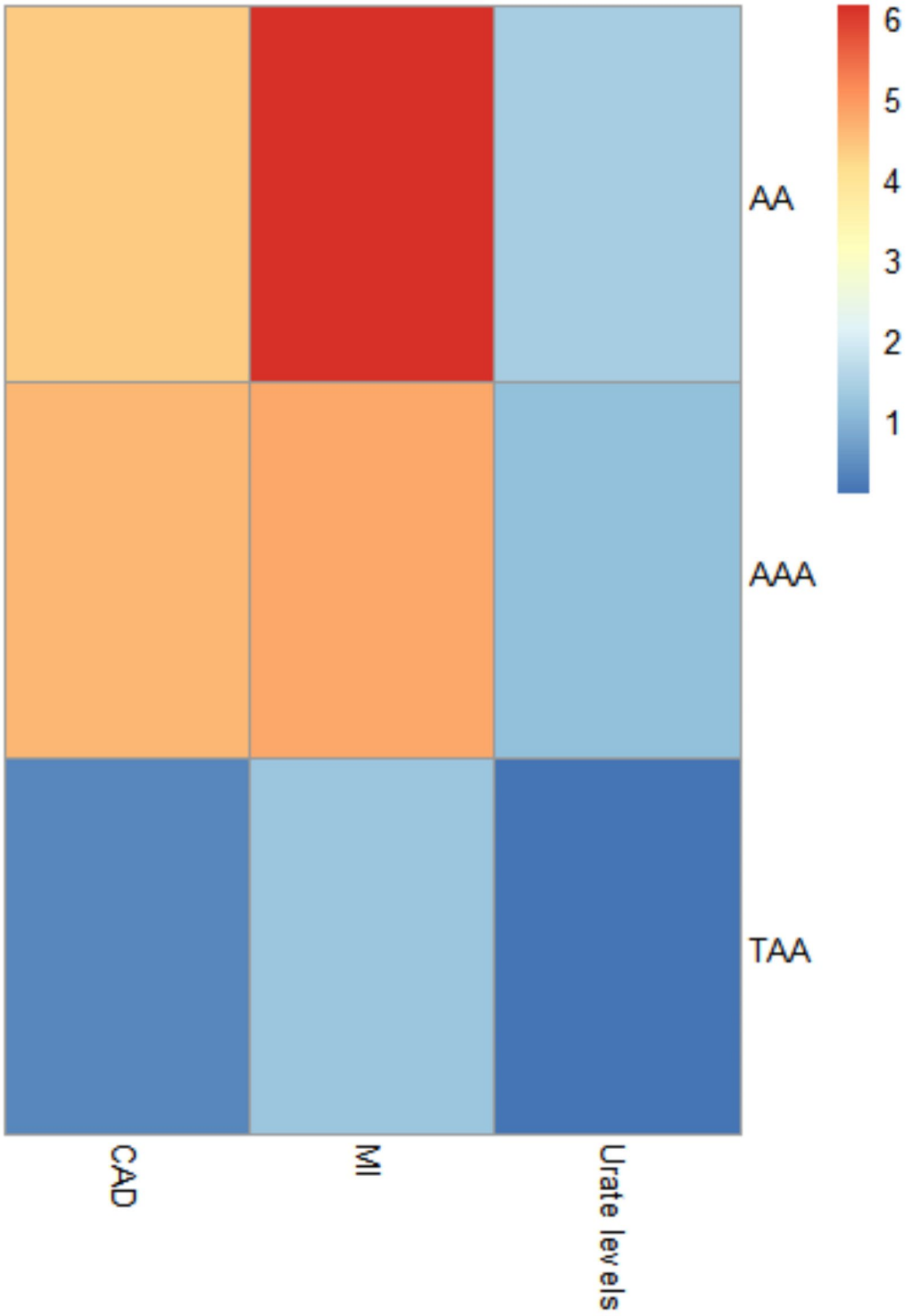

Fig. 2. Displays the association among CAD/MI, urate levels, and AA/AAA/TAA.

Sensitivity analysis

Figures 3, 4 and 5 displays the scatter plot illustrating the effect sizes of SNPs in relation to CAD, MI, urate levels, and AA. Figures 6 and 7 displays the scatter plot illustrating the effect sizes of SNPs in relation to CAD, MI, and AAA. The IVW test for heterogeneity indicated the absence of heterogeneity in the MR research findings pertaining to the relationship between urate levels and AA. The IVW test for heterogeneity and MR-PRESSO global test yielded significant evidence ($p < 0.05$) indicating the presence of heterogeneity in the results of the MR analysis conducted on CAD, MI, and AA, AAA, respectively(Table 2). The regression results conducted by MR-Egger indicated the absence of pleiotropy for mostly MR analysis, with a p-value greater than 0.05 (Table 2). The Supplementary Figures S1-S4 display the MR outcome pertaining to CAD, MI, and TAA, AD, respectively.

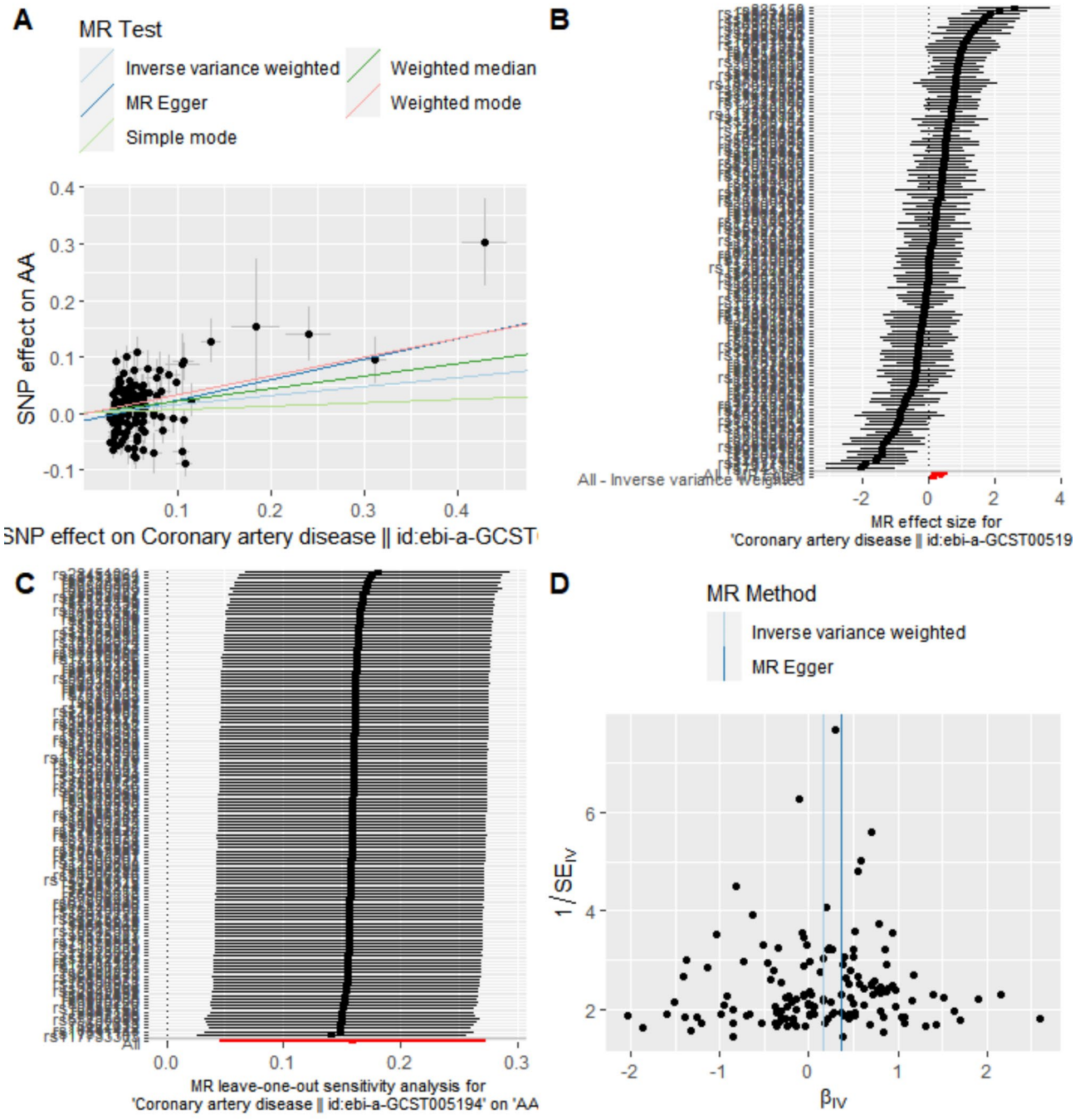

Fig. 3. Presents the MR outcomes pertaining to CAD and AA. Subfigure A displays a scatter plot illustrating the genetic correlations between CAD and AA; Subfigure B showcases a forest plot of the causal effects of CAD associated SNPs on AA.Subfigure C showcases a leave-one-out plot of the causal effects of CAD associated SNPs on AA.Subfigure D showcases a funnel plot of the causal effects of CAD associated SNPs on AA.

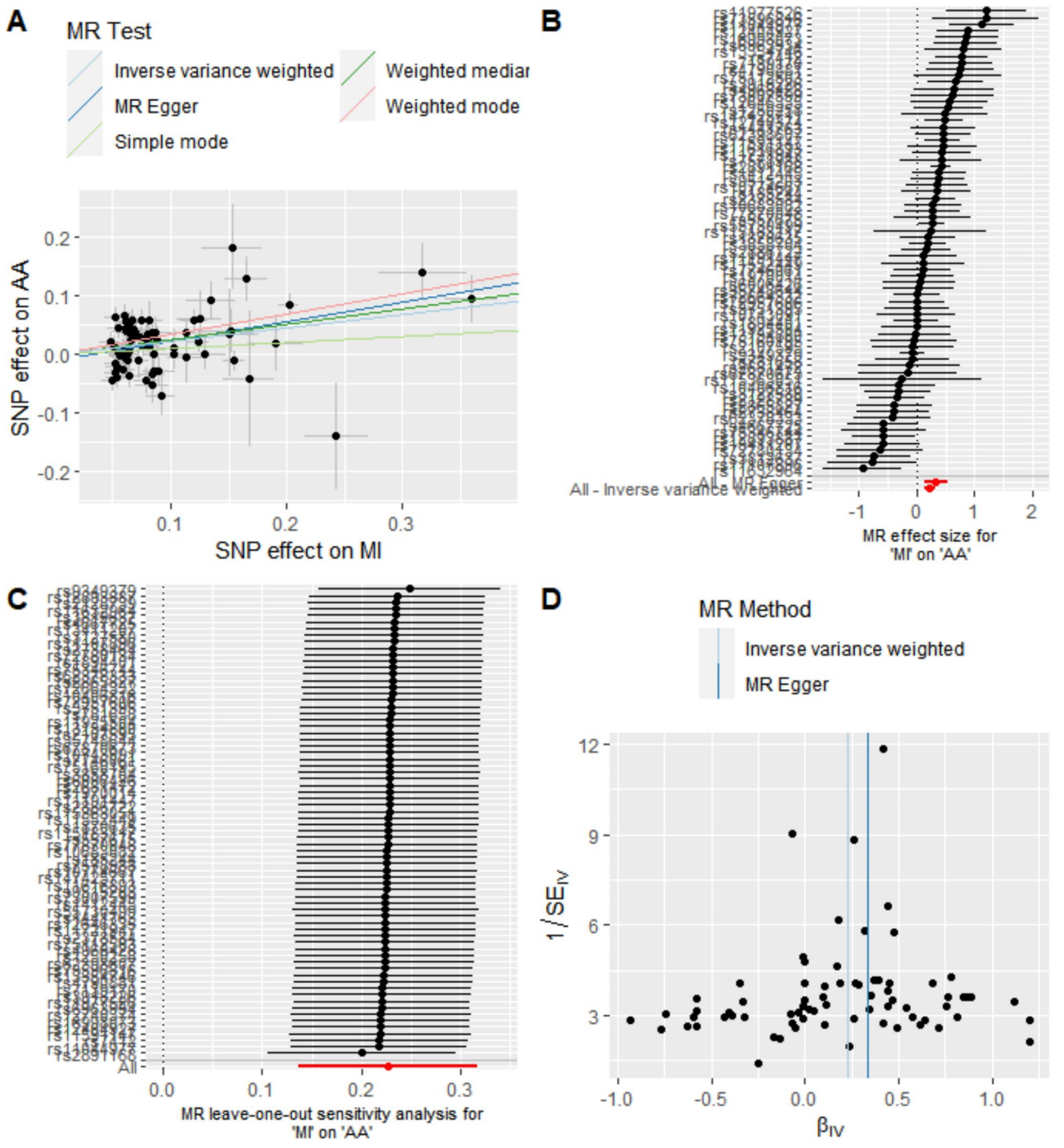

Fig. 4. Presents the MR outcomes pertaining to MI and AA. Subfigure A displays a scatter plot illustrating the genetic correlations between MI and AA; Subfigure B showcases a forest plot of the causal effects of MI associated SNPs on AA.Subfigure C showcases a leave-one-out plot of the causal effects of MI associated SNPs on AA.Subfigure D showcases a funnel plot of the causal effects of MI associated SNPs on AA.

Discussion

This study employed a two-sample Mendelian randomization technique to examine the genetic linkages between CAD, MI, urate levels, and the risks of AA, AAA, TAA and AD. Our investigation has contributed novel evidence that supports the prior clinical observations regarding the causative association between the presence of CAD/MI and an increased risk of AA/AAA. Furthermore, our findings have provided novel insights by demonstrating, for the first time, that the genetic predisposition to CAD/MI and the susceptibility to TAA are not causally linked, as determined from the analysis of the same GWAS datasets.

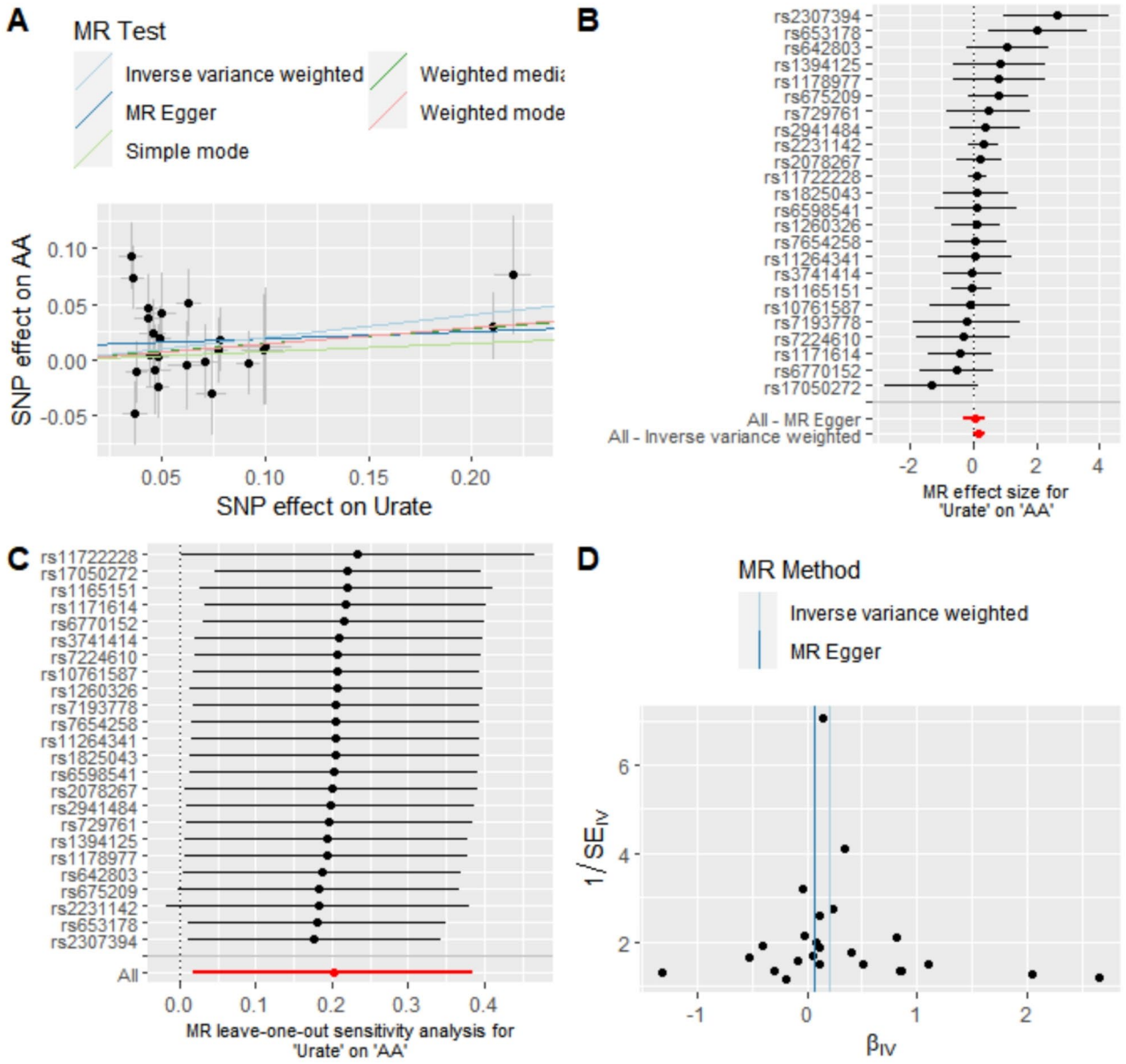

Fig. 5. Presents the MR outcomes pertaining to urate levels and AA. Subfigure A displays a scatter plot illustrating the genetic correlations between urate levels and AA; Subfigure B showcases a forest plot of the causal effects of urate levels associated SNPs on AA.Subfigure C showcases a leave-one-out plot of the causal effects of urate levels associated SNPs on AA.Subfigure D showcases a funnel plot of the causal effects of urate levels associated SNPs on AA.

The initial meta-analysis conducted by Cornuz et al. demonstrated that a previous occurrence of CAD was a significant risk factor or indicator for the detection of AAA through screening (OR, 2.30; 95%CI, 1.92 to 2.75)[27]. A recent meta-analysis conducted by Li et al. demonstrated that CAD was found to be a significant risk factor for AAA(OR, 1.82; 95% CI, 1.65 to 2.00)[28]. Notwithstanding the evidence supporting the positive correlation between CAD and the occurrence of AAA, it is worth noting that CAD cannot be related with AAA growth[29], or it may even exhibit a negative association[30]. The combined analysis of all 20 studies revealed a statistically significant inverse relationship between CAD and the rate of AAA expansion in the fixed-effect model. However, this link was no longer present when using the pooled random-effects modeling approach[7]. Takagi et al.[31,32] proposed that CAD exhibited a positive correlation with the presence of AAA, perhaps had a negative correlation with the expansion of AAA, and might potentially have no correlation with the rupture of AAA. The research study discovered that the occurrence of asymptomatic, clinically relevant CAD in individuals with AAA was determined to be as high as 61% [33]. In a similar vein, Long et al. conducted a study which revealed a higher incidence of AAA among individuals with a prior medical history of acute coronary events and obstructive CAD[34]. This study identified a causal association between CAD/MI and AA/AAA, maybe by virtue

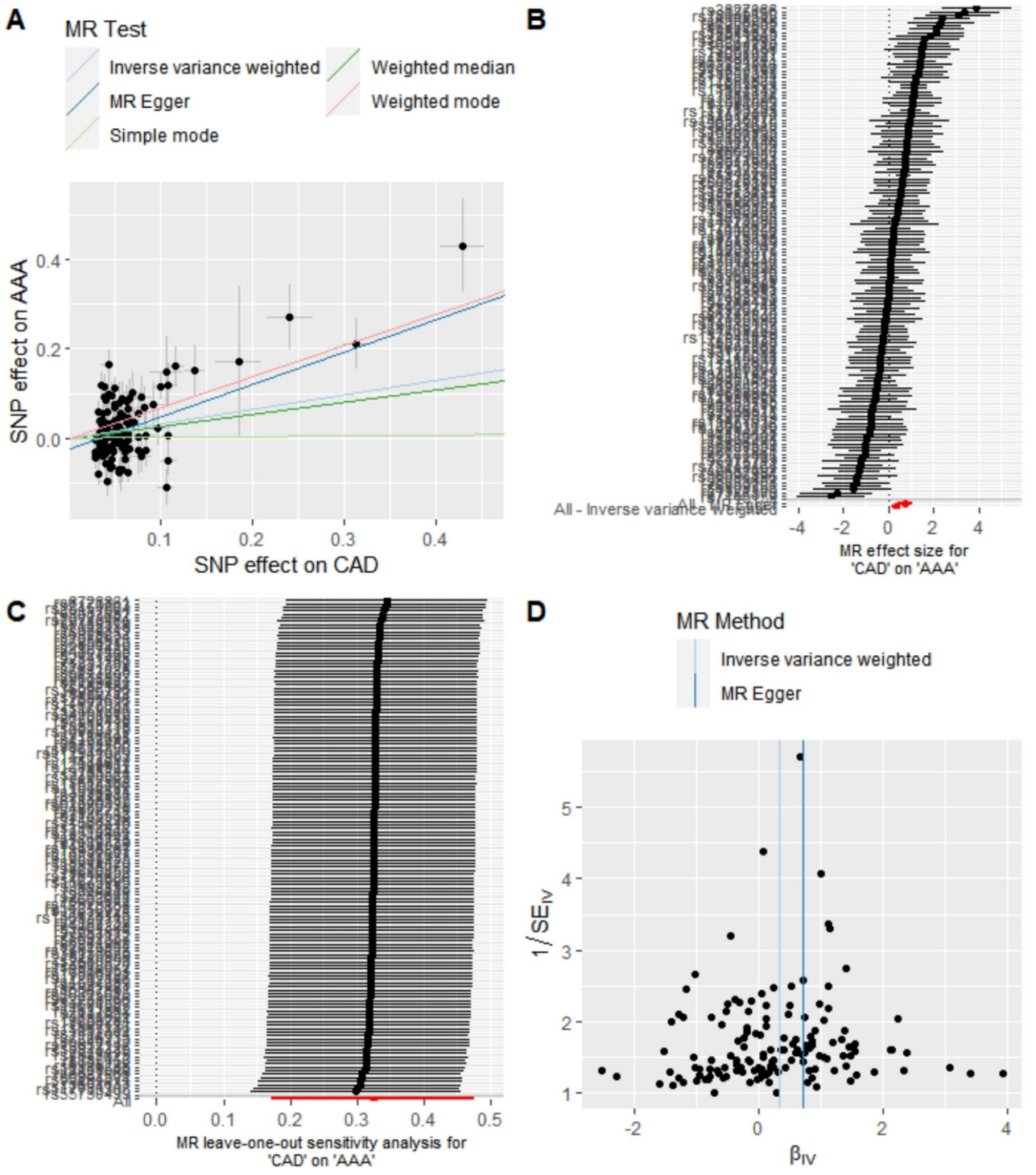

Fig. 6. Presents the MR outcomes pertaining to CAD and AAA. Subfigure A displays a scatter plot illustrating the genetic correlations between CAD and AAA; Subfigure B showcases a forest plot of the causal effects of CAD associated SNPs on AAA.Subfigure C showcases a leave-one-out plot of the causal effects of CAD associated SNPs on AAA.Subfigure D showcases a funnel plot of the causal effects of CAD associated SNPs on AAA.

of their shared pathophysiological base (atherosclerosis) and overlapping risk variables. Nevertheless, further investigation is required to elucidate the precise process. Based on these data, it may be inferred that early-stage assessment of coronary arteries should be conducted in all patients diagnosed with AA[35]. Also, it is imperative to do screening for AA or AAA in individuals diagnosed with CAD or MI.

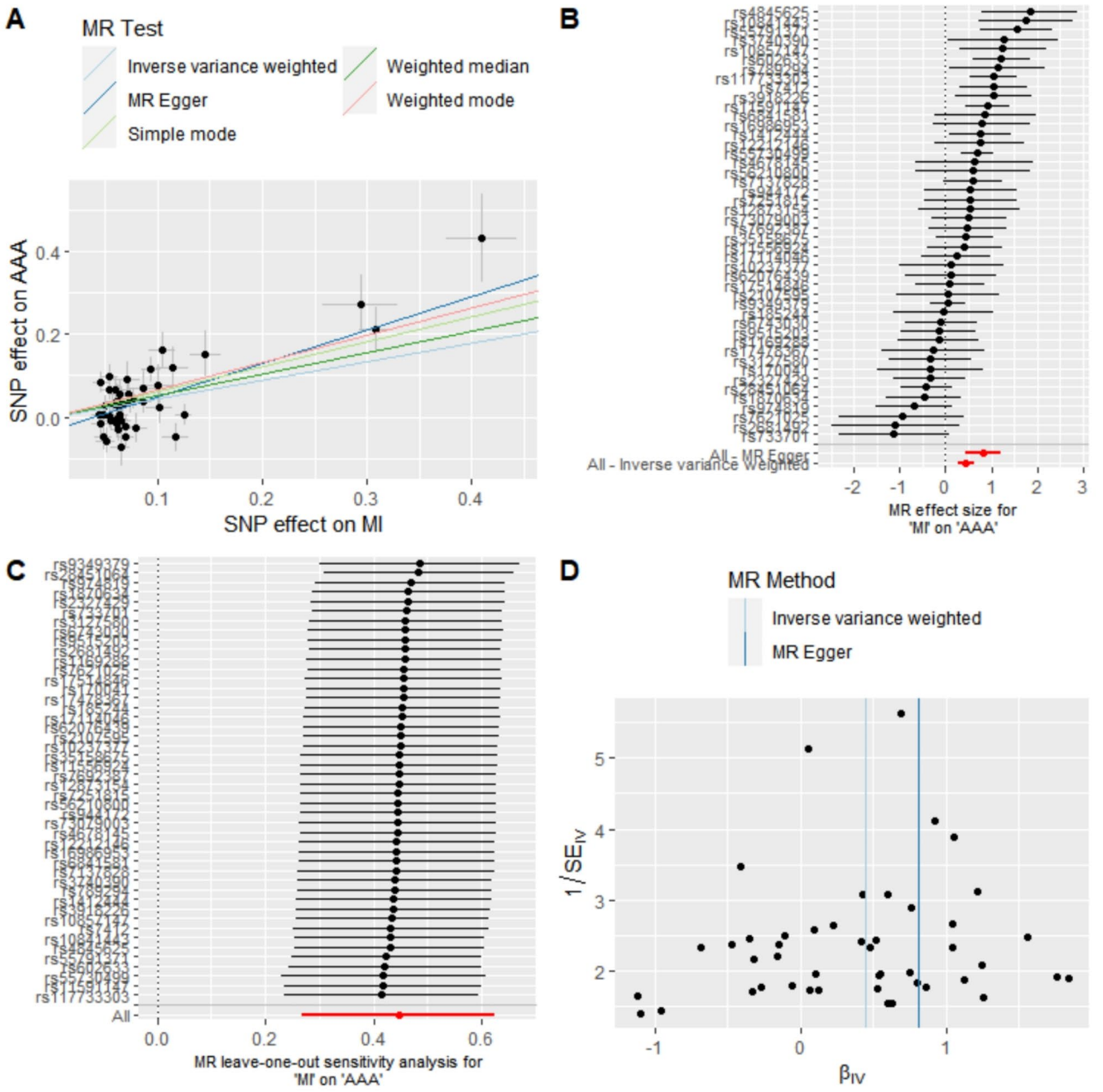

Fig. 7. Presents the MR outcomes pertaining to MI and AAA. Subfigure A displays a scatter plot illustrating the genetic correlations between MI and AAA; Subfigure B showcases a forest plot of the causal effects of MI associated SNPs on AAA.Subfigure C showcases a leave-one-out plot of the causal effects of MI associated SNPs on AAA.Subfigure D showcases a funnel plot of the causal effects of MI associated SNPs on AAA.

Regarding urate, it serves as an indicator of oxidative stress. A study conducted by Ali et al. has demonstrated a clear correlation between levels of urate and the diameter of the aorta[36]. In the mouse model of thoracic aortic aneurysm and dissection, the administration of a 4-week adenine diet resulted in the direct induction of thoracic aortic aneurysm and dissection formation. This was evidenced by the observed rise in maximal thoracic aortic diameters and significant elastin degradation. However, the negative effects were mitigated by the administration of allopurinol[37]. In a similar vein, the research demonstrates that the xanthine oxidoreductase inhibitor allopurinol disrupts the progression of AA by functioning as a robust antioxidant. This finding provides more evidence that redox stress is important for the growth and progression of AA[38]. According to a study conducted on animals, there is evidence to suggest that hyperuricemia could potentially contribute to the development of AAA. The study also proposes that the URAT1/ERK1/2/MMP-9 pathway may be one of the potential mechanisms involved in the pathogenesis of AAA[39]. According to a population-based study conducted in Taiwan, patients diagnosed with gout demonstrated a notable increase in the occurrence of AAA development. The study, which spanned a period of 14 years, utilized data from the National Health Insurance

Outcome	Exposure	Method	nsnp	F-statistic	pval	OR(95%CI)	Q statistic	Q_pval	Egger_intercept_p	Presso_global_p
AA	Coronary artery disease	IVW	137	76.369	4.29e-05	1.309(1.150–1.490)	222.538	4.06e-06	0.061	< 0.0003
		MR Egger	137		4.21e-04	1.647(1.257–2.158)				
		Weighted mode	137		4.95e-03	1.446 (1.123–1.862)				
		Weighted median	137		8.44e-04	1.367(1.137–1.643)				
	Myocardial infarction	IVW	72	65.407	7.60e-07	1.255(1.147–1.373)	175.817	7.27e-11	0.264	< 5e-04
		MR Egger	72		2.12e-03	1.394 (1.137–1.709)				
		Weighted mode	72		9.07e-06	1.414(1.227–1.630)				
		Weighted median	72		6.75e-07	1.300(1.1724–1.442)				
	Urate levels	IVW	24	253.202	0.039	1.178(1.008–1.377)	30.272	0.142	0.262	0.202
		MR Egger	24		0.558	1.070(0.855-1.400)				
		Weighted mode	24		0.214	1.119(0.941–1.330)				
		Weighted median	24		0.329	1.093(0.914–1.308)				
AAA	Coronary artery disease	IVW	141	68.930	2.67e-05	1.383(1.189–1.609)	391.462	1.18e-25	0.011	< 0.0003
		MR Egger	141		4.53e-05	2.056 (1.470–2.876)				
		Weighted mode	141		1.92e-03	2.001(1.302–3.077)				
		Weighted median	141		1.30e-03	1.310(1.111–1.545)				
	Myocardial infarction	IVW	73	58.854	1.82e-05	1.352(1.178–1.552)	191.586	8.39e-13	0.806	< 5e-04
		MR Egger	73		4.90e-02	1.404 (1.007–1.960)				
		Weighted mode	73		3.04e-01	1.189(0.856–1.650)				
		Weighted median	73		5.05e-04	1.308(1.124–1.521)				
TAA	Coronary artery disease	IVW	139	76.053	0.439	1.047 (0.932–1.178)	252.670	9.33e-09	0.658	< 0.0003
		MR Egger	139		0.451	1.101 (0.858–1.412)				
		Weighted mode	139		0.765	0.970(0.796–1.182)				
		Weighted median	139		0.889	1.011(0.864–1.183)				
	Myocardial infarction	IVW	69	65.407	0.058	1.101 (0.997–1.216)	100.803	0.006	0.259	0.005
		MR Egger	69		0.857	0.979 (0.783–1.226)				
		Weighted mode	69		0.946	0.995(0.856–1.156)				
		Weighted median	69		0.735	1.023(0.896–1.168)				
AD	Coronary artery disease	IVW	142	76.053	0.375	1.098(0.893–1.351)	209.530	0.0002	0.254	< 0.0003
		MR Egger	142		0.155	1.377(0.888–2.137)				
		Weighted mode	142		0.189	1.297(0.882–1.908)				
		Weighted median	142		0.391	1.133(0.852–1.505)				
	Myocardial infarction	IVW	73	65.407	0.198	1.130(0.938–1.360)	98.483	0.021	0.494	< 0.0003
		MR Egger	73		0.241	1.290(0.846–1.967)				
		Weighted mode	73		0.332	1.184(0.844–1.662)				
		Weighted median	73		0.113	1.225(0.953–1.576)				

Table 2. MR estimates for determining the relationship between CAD, MI, urate levels and AA, AAA, TAA, AD.

Research Database. The results indicated that the adjusted hazard ratio (HR) for AAA development in patients with gout was 2.465, with a p-value of less than 0.001. Furthermore, the study found that patients who received treatment with anti-gout medications had a significantly reduced risk of being diagnosed with AAA compared to those who did not receive such treatment. The adjusted HR for this group was 0.489, with a p-value of less than 0.001[8]. According to a retrospective study, it was observed that individuals with blood urate levels over 9 mg/dl had greater rates of AAA expansion compared to those with serum urate levels ranging from 4 to 7.9 mg/dl[39]. There is evidence indicating that elevated levels of urate in the bloodstream have a direct impact on the promotion of oxidative stress. According to recent studies, ascending AA may be significantly influenced by oxidative stress[36]. According to a meta-analysis, there is substantial data indicating that individuals with AD exhibit considerably elevated levels of blood urate[40]. The general population was found to have an increased risk of AD-related death as a result of hyperuricemia[41]. The research discovered that serum urate was a significant predictor of unfavorable prognosis in individuals diagnosed with type A acute aortic dissection[42]. The present study has identified a causal association between levels of urate and AA, however, after Bonferroni correction, the causal relationship between the levels of urate and AA lost statistical significance. Therefore, further research is needed to investigate the causal relationship between them. Additionally, no causative link between urate and AAA, TAA or AD was established in this investigation. Moreover, due to the small number of AD, the relationship between urate level and AD still needs further research.

Strengths and limitations

In contrast to conventional observational studies, our analysis effectively addressed the potential impact of residual confounding factors and reverse causality, hence bolstering the robustness and validity of our findings. Also, deriving CAD/MI summary statistics from UK Biobank, urate summary statistics from GUGC, and AA/AD summary statistics from FinnGen could avoid potential bias from sample overlap[43]. Nevertheless, it is important to acknowledge various constraints inherent in our research. The GWAS data utilized in our investigation were exclusively sourced from the Europe. Hence, the generalizability of our findings to other ethnic groups necessitates additional investigation. Furthermore, due to the limited number of AD cases, it may have an impact on the results. Ultimately, despite the absence of any empirical support for pleiotropic effects in the MR-Egger intercept tests conducted in our work, it remains challenging to entirely rule out the potential impact of directional pleiotropy.

Conclusion

In summary, our investigation has established a causal association between genetically determined CAD/MI, and the susceptibility to AA/AAA. Additionally, our study has discovered, for the first time, that genetically determined CAD, MI, and urate levels do not impact the risk of TAA. These findings have significant implications for informing clinical prevention strategies, designing clinical trials, and conducting risk-factor analysis pertaining to AA and AD.

Data availability

All data can be obtained from IEU OpenGWAS project(mrcieu.ac.uk) and FinnGenwebsite (https://www.finngen.fi/en/access_results).

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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Correspondence and requests for materials should be addressed to T.X.