Supplementary

Table S1 Six SNPs were selected as IVs for serum MMP-12 levels

Chr	Pos	Beta	SE	P value	Sample size	ID	SNP	Effect allele	Other allele	EAF	Exposure
11	102684935	0.155	0.0112	1.46E–43	21,758	ebi-a-GCST90012070	rs1144398	G	T	0.2967	MMP-12 levels
	102839201	0.110	0.0161	1.00E–11	21,758	ebi-a-GCST90012070	rs7126430	A	G	0.1256	MMP-12 levels
	102275937	–0.304	0.0521	5.22E–09	21,758	ebi-a-GCST90012070	rs181951510	A	G	0.0182	MMP-12 levels
	102720945	–0.474	0.0127	1.00E–200	21,758	ebi-a-GCST90012070	rs626750	A	G	0.1898	MMP-12 levels
	102787451	0.280	0.0139	2.18E–90	21,758	ebi-a-GCST90012070	rs12288698	C	T	0.1737	MMP-12 levels
13	72450627	0.254	0.0461	3.42E–08	21,758	ebi-a-GCST90012070	rs117953762	C	T	0.0192	MMP-12 levels

Chr, chromosome; EAF, effector allele frequency; IV, instrumental variable; MMP-12, matrix metalloproteinase-12; pos, position; SE, standard error; SNP, single-nucleotide polymorphism.

Table S2 Three gene variants were selected as IVs of AD

Chr	Pos	Beta	SE	P value	Sample size	ID	SNP	Effect allele	Other allele	EAF	Exposure
7	145366398	0.7956	0.1631	1.07E–06	207,011	finn-b-I9_AORTDIS	rs118055578	A	G	0.04923	AD
12	15673103	0.4052	0.0869	3.13E–06	207,011	finn-b-I9_AORTDIS	rs2302688	T	C	0.1821	AD
15	48027465	1.3977	0.2822	7.31E–07	207,011	finn-b-I9_AORTDIS	rs145146588	C	T	0.01829	AD

AD, aortic dissection; chr, chromosome; EAF, effector allele frequency; IV, instrumental variable; pos, position; SE, standard error; SNP, single-nucleotide polymorphism.

Table S3 Four gene variants were selected as IVs of AA

Chr	Pos	Beta	SE	P value	Sample size	ID	SNP	Effect allele	Other allele	EAF	Exposure
1	218668879	0.3621	0.0691	1.60E–07	209,366	finn-b-I9_AORTANEUR	rs12406058	A	G	0.04529	AA
10	95910761	0.2157	0.0417	2.37E–07	209,366	finn-b-I9_AORTANEUR	rs79958663	T	C	0.1313	AA
12	26545147	0.2142	0.0418	3.03E–07	209,366	finn-b-I9_AORTANEUR	rs61914381	A	G	0.1356	AA
13	22861921	–0.1949	0.0347	1.96E–08	209,366	finn-b-I9_AORTANEUR	rs9316871	G	A	0.2063	AA

AA, aortic aneurysm; chr, chromosome; EAF, effector allele frequency; IV, instrumental variable; pos, position; SE, standard error; SNP, single-nucleotide polymorphism.

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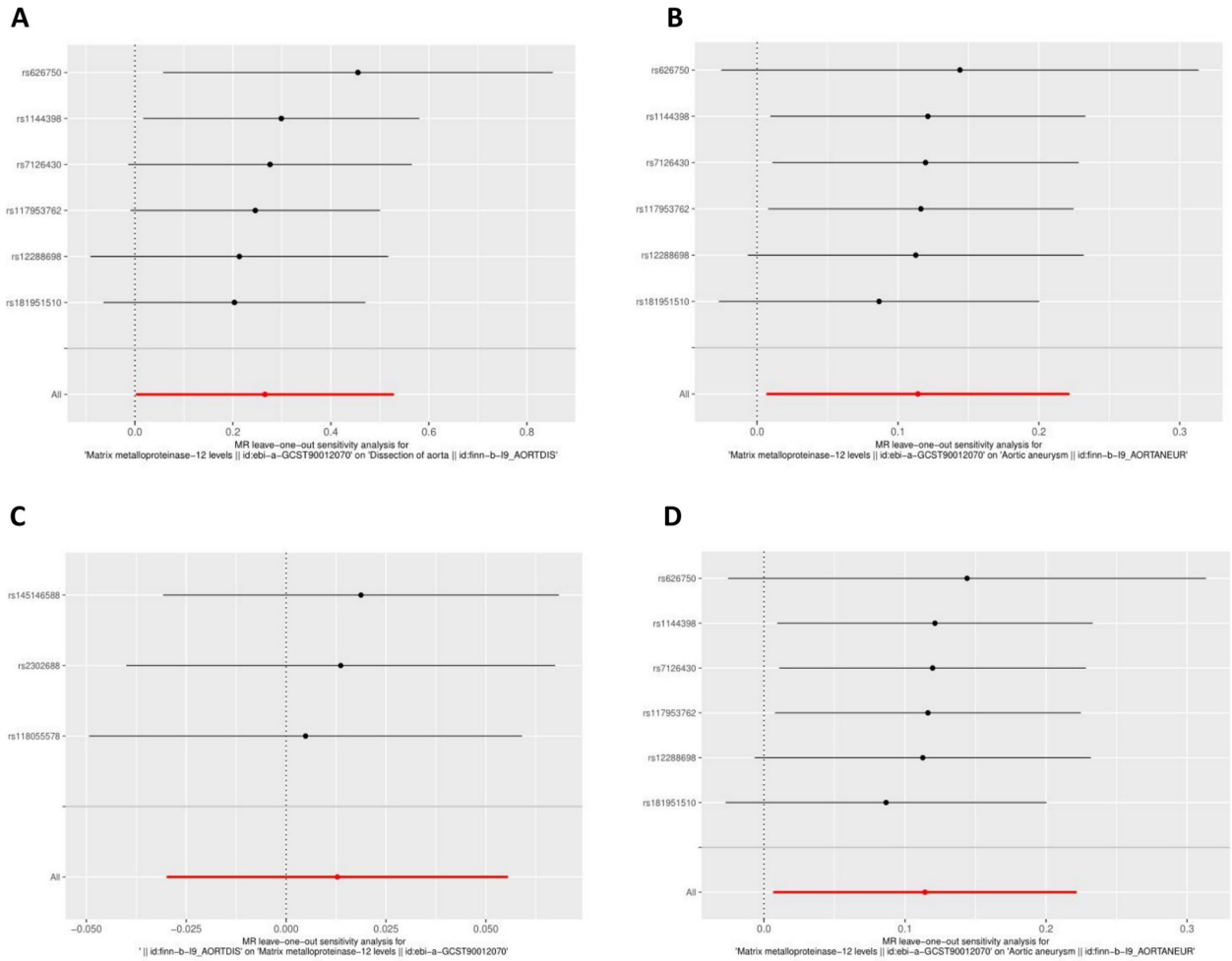

Figure S1 Forest plots for leave-one-out analysis of the causal relationship between MMP-12 and AD or AA. (A) MR leave-one-out analysis for serum MMP-12 levels on AD. (B) MR leave-one-out analysis for serum MMP-12 levels on AA. (C) MR leave-one-out analysis for AD on serum MMP-12 levels. (D) MR leave-one-out analysis for AA on serum MMP-12 levels. AA, aortic aneurysm; AD, aortic dissection; MMP-12, matrix metalloproteinase-12; MR, Mendelian randomization.

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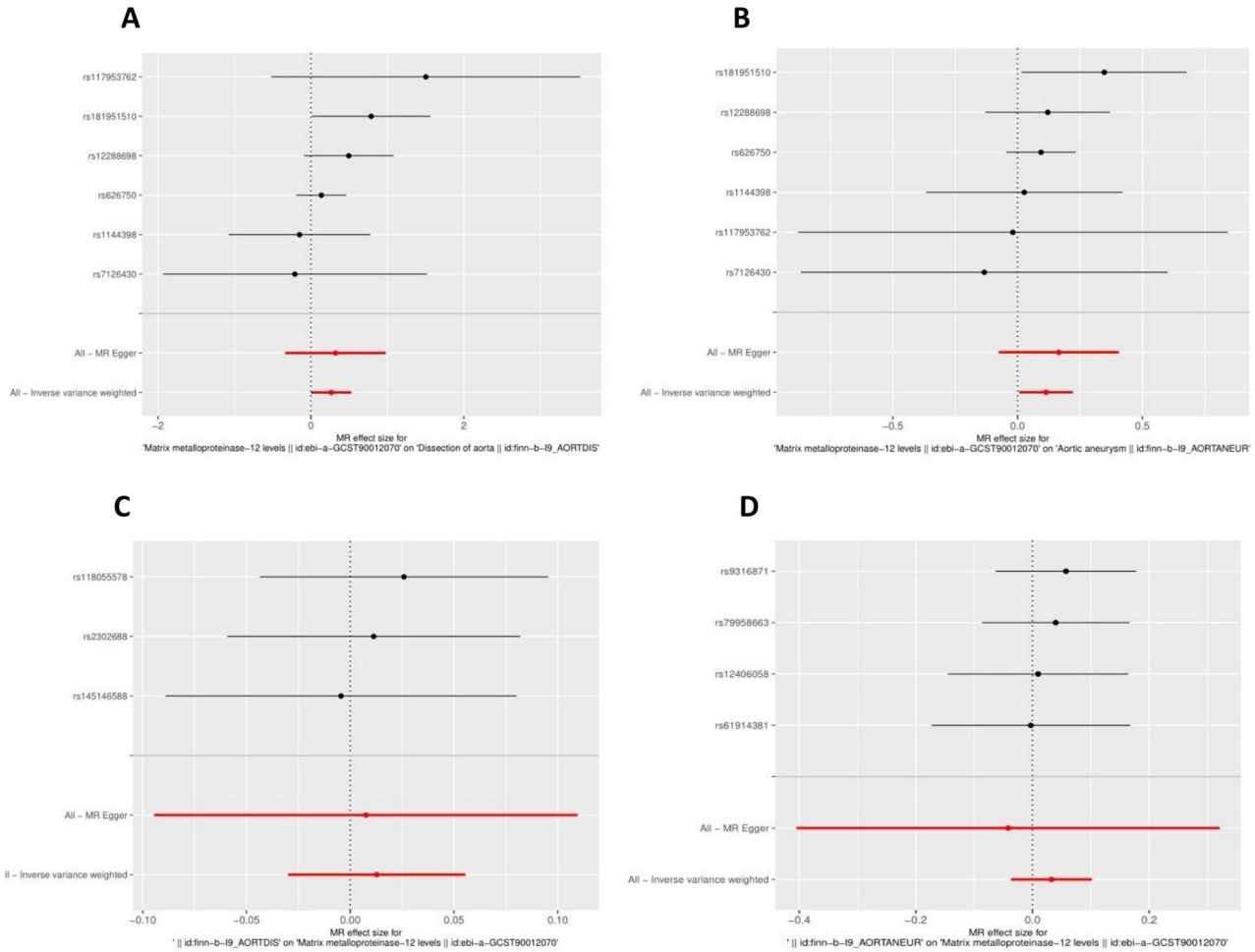

Figure S2 Forest plots of the causal relationship between MMP-12 and AD or AA. (A) MR effect size for serum MMP-12 levels on AD. (B) MR effect size for serum MMP-12 levels on AA. (C) MR effect size for AD on serum MMP-12 levels. (D) MR effect size for AA on serum MMP-12 levels. AA, aortic aneurysm; AD, aortic dissection; MMP-12, matrix metalloproteinase-12; MR, Mendelian randomization.

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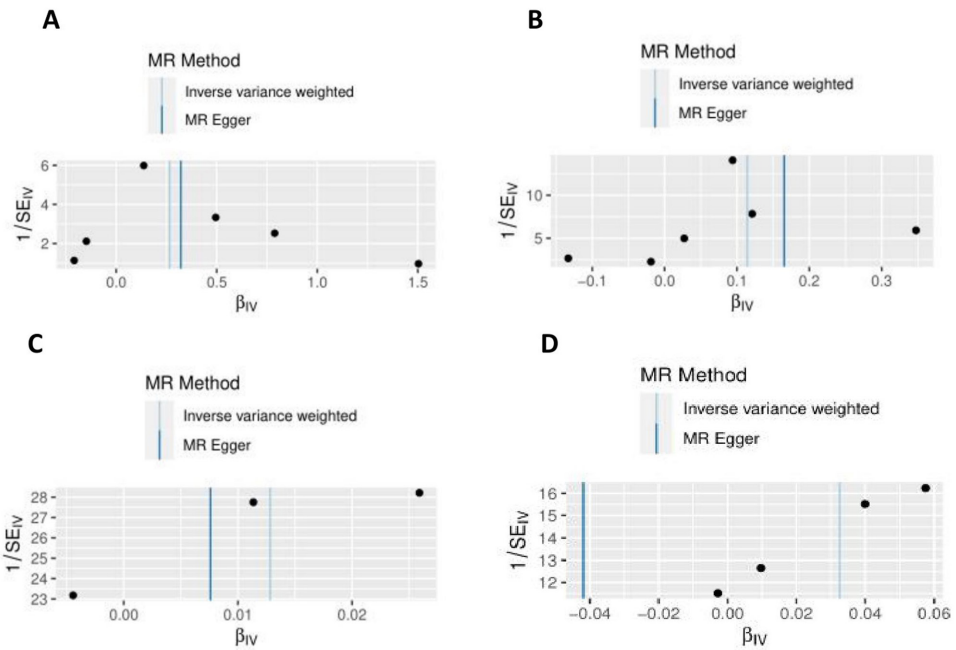

Figure S3 Funnel plots of the causal relationship between MMP-12 and AD or AA. (A) Funnel plot for serum MMP-12 levels on AD. (B) Funnel plot for serum MMP-12 levels on AA. (C) Funnel plot for AD on serum MMP-12 levels. (D) Funnel plot for AA on serum MMP-12 levels. AA, aortic aneurysm; AD, aortic dissection; IV, instrumental variable; MMP-12, matrix metalloproteinase-12; MR, Mendelian randomization; SE, standard error.

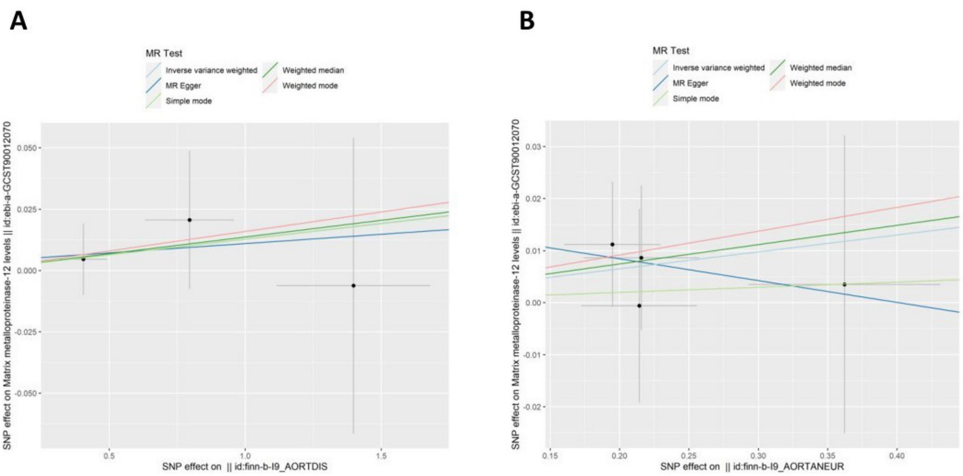

Figure S4 Scatter plots of the causal relationship between AD or AA and MMP-12. (A) Scatter plot of the causal effect of AD on MMP-12 levels. (B) Scatter plot of the causal effect of AA on MMP-12 levels. AA, aortic aneurysm; AD, aortic dissection; MMP-12, matrix metalloproteinase-12; MR, Mendelian randomization; SNP, single-nucleotide polymorphism.

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