Supplementary Material

Genetic variants associated with NAFLD do not associate with measures of sub-clinical atherosclerosis. Results from the IMPROVE study

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2. Ethics

The study was designed in accordance with the rules of Good Clinical Practice, and with the ethical principles established in the Declaration of Helsinki. Each participant provided two different informed consents; one for general participation in the study and one for genotyping. The study was approved by the Institutional Review Board (IRB) at each one of the seven recruiting centers: (1) the Regional Ethics Review Board at Karolinska Institutet, Stockholm Sweden, (2) IRB at the Groupe Hôpitalier Pitie-Salpetriere, Paris, France, (3) the IRB Comitato Etico delle Aziende Sanitarie della regione Umbria, Perugia and (4) the IRB at the Ospedale Niguarda Ca´Granda, Milano, both in Italy, (5) the IRB at the University Hospital Groningen, Groningen, the Netherlands, (6) the IRB Hospital District of Northern Savo and (7) and the IRB at University of Eastern Finland, both in Kuopio, Finland. Each participant provided two different written consents one for general participation in the study and one for genotyping.

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Supplementary Table S1. Distribution of c-IMT and ICCAD measures across rs738409 (C/G), rs10401969 (T/C), and rs1260326 (C/T) genotype groups in the different ALT quartiles.

Quartile	*n*		rs738409			rs10401969		rs1260326		
			CC	**CG**	**GG**	**TT**	**CT+CC**	**CC**	**CT**	**TT**
			(*n*=623)	**(*n*=227)**	**(*n*=26)**	**(*n*=786)**	**(*n*=90)**	**(*n*=265)**	**(*n*=433)**	**(*n*=178)**
I	876	$c\text{-}IMT_{mean}$	0.85	0.87	0.78	0.85	0.85	0.86	0.85	0.83
			(0.74-0.99)	(0.73-1.01)	(0.73-0.95)	(0.74-1.00)	(0.70-0.97)	(0.75-0.99)	(0.75-1.00)	(0.72-0.98)
		$c\text{-}IMT_{max}$	1.85	1.94	1.8	1.88	1.84	1.93	1.85	1.85
			(1.45-2.55)	(1.45-2.61)	(1.39-2.31)	(1.45-2.59)	(1.39-2.42)	(1.45-2.55)	(1.45-2.59)	(1.39-2.41)
		$c\text{-}IMT_{mean\text{-}max}$	1.21	1.22	1.13	1.21	1.22	1.23	1.22	1.17
			(1.04-1.41)	(1.04-1.48)	(1.00-1.36)	(1.04-1.42)	(1.04-1.41)	(1.05-1.42)	(1.05-1.42)	(1.02-1.42)
		ICCAD	7.68	7.8	7.27	7.68	7.81	7.79	7.64	7.64
			(7.17-8.27)	(7.20-8.30)	(6.92-7.89)	(7.15-8.24)	(7.22-8.34)	(7.20-8.25)	(7.15-8.30)	(7.10-8.15)
			CC	**CG**	**GG**	**TT**	**CT+CC**	**CC**	**CT**	**TT**
			(*n*=632)	**(*n*=274)**	**(*n*=23)**	**(*n*=827)**	**(*n*=102)**	**(*n*=279)**	**(*n*=413)**	**(*n*=237)**
II	929	$c\text{-}IMT_{mean}$	0.85	0.85	0.88	0.85	0.84	0.86	0.85	0.84
			(0.74-0.98)	(0.76-0.99)	(0.74-1.04)	(0.75-0.98)	(0.74-1.03)	(0.74-1.02)	(0.75-0.97)	(0.74-0.98)
		$c\text{-}IMT_{max}$	1.85	1.88	1.93	1.85	1.84	1.85	1.85	1.85
			(1.45-2.50)	(1.39-2.42)	(1.48-2.42)	(1.45-2.42)	(1.39-2.61)	(1.45-2.61)	(1.48-2.42)	(1.39-2.41)
		$c\text{-}IMT_{mean\text{-}max}$	1.18	1.16	1.22	1.18	1.2	1.2	1.18	1.16
			(1.05-1.39)	(1.05-1.41)	(1.00-1.54)	(1.05-1.39)	(1.07-1.45)	(1.05-1.45)	(1.05-1.37)	(1.03-1.38)
		ICCAD	7.67	7.79	7.89	7.69	7.8	7.81	7.69	7.6
			(7.18-8.24)	(7.28-8.34)	(7.11-8.30)	(7.21-8.27)	(7.22-8.38)	(7.27-8.35)	(7.21-8.27)	(7.17-8.24)
			CC	**CG**	**GG**	**TT**	**CT+CC**	**CC**	**CT**	**TT**
			(*n*=546)	**(*n*=235)**	**(*n*=20)**	**(*n*=691)**	**(*n*=110)**	**(*n*=253)**	**(*n*=373)**	**(*n*=175)**
III	801	$c\text{-}IMT_{mean}$	0.85	0.86	0.87	0.85	0.87	0.86	0.85	0.85
			(0.74-0.98)	(0.73-1.01)	(0.75-0.94)	(0.73-1.00)	(0.76-1.03)	(0.74-1.00)	(0.73-0.99)	(0.74-1.02)

		c-IMT$_{max}$	1.84	1.85	1.8	1.84	1.85	1.85	1.76	1.85
			(1.39-2.41)	(1.39-2.51)	(1.42-2.59)	(1.39-2.41)	(1.48-2.51)	(1.45-2.5)	(1.39-2.32)	(1.35-2.5)
		c-IMT$_{mean-max}$	1.2	1.18	1.2	1.19	1.23	1.22	1.18	1.2
			(1.02-1.42)	(1.03-1.41)	(1.07-1.33)	(1.02-1.40)	(1.06-1.49)	(1.03-1.42)	(1.02-1.38)	(1.03-1.45)
		ICCAD	7.68	7.78	7.8	7.73	7.78	7.84	7.64	7.64
			(7.19-8.33)	(7.22-8.29)	(7.33-8.12)	(7.20-8.27)	(7.20-8.46)	(7.31-8.48)	(7.14-8.16)	(7.21-8.29)
			CC	**CG**	**GG**	**TT**	**CT+CC**	**CC**	**CT**	**TT**
			(*n*=453)	**(*n*=249)**	**(*n*=39)**	**(*n*=631)**	**(*n*=110)**	**(*n*=273)**	**(*n*=330)**	**(*n*=178)**
IV	741	c-IMT$_{mean}$	0.84	0.85	0.78	0.83	0.88	0.86	0.85	0.82
			(0.73-0.99)	(0.76-1.00)	(0.71-0.88)	(0.73-1.00)	(0.78-1.01)	(0.76-1.00)	(0.73-1.02)	(0.74-0.95)
		c-IMT$_{max}$	1.84	1.94	1.67	1.78	2.13	1.93	1.85	1.74
			(1.36-2.50)	(1.45-2.59)	(1.20-2.22)	(1.35-2.50)	(1.67-2.61)	(1.45-2.51)	(1.35-2.59)	(1.39-2.31)
		c-IMT$_{mean-max}$	1.19	1.23	1.1	1.18	1.26	1.23	1.19	1.16
			(1.02-1.40)	(1.04-1.44)	(0.98-1.28)	(1.01-1.39)	(1.11-1.48)	(1.05-1.43)	(1.01-1.44)	(1.02-1.36)
		ICCAD	7.87	7.92	7.56	7.87	7.84	7.97	7.8	7.72
			(7.34-8.44)	(7.33-8.46)	(7.11-8.09)	(7.32-8.42)	(7.35-8.51)	(7.35-8.56)	(7.34-8.41)	(7.21-8.31)

Data are reported as median and IQR. Minor allele frequency (%) for each quartile (Q): rs738409-G Q1:16, Q2:17, Q3:17, Q4:22; rs10401969-C Q1:5, Q2:5, Q3:7, Q4:8; rs1260326-T Q1:45, Q2:47, Q3:45, Q4:44. Abbreviations: *n* number of subjects

Supplementary Table S2. Association of rs10401969 (T/C) with measures of c-IMT and ICCAD in the different ALT quartiles.

ù	*n*	Ultrasonographic measures	Model 1			Model 2		
			β	SE	*p*	β	SE	*p*
I	876	c-IMT $_{mean}$	0.003	0.013	0.765	-0.004	0.009	0.667
		c-IMT $_{max}$	-0.01	0.019	0.574	-0.021	0.011	0.224
		c-IMT $_{mean-max}$	0.002	0.011	0.847	-0.006	0.01	0.559
		ICCAD	0.005	0.005	0.309	0.002	0.004	0.697
II	929	c-IMT $_{mean}$	0.003	0.009	0.704	-0.008	0.008	0.317
		c-IMT $_{max}$	0	0.168	1	-0.015	0.016	0.33
		c-IMT $_{mean-max}$	0.006	0.01	0.558	-0.007	0.009	0.432
		ICCAD	0.005	0.005	0.275	-0.001	0.004	0.866
III	801	c-IMT $_{mean}$	0.012	0.009	0.177	0.003	0.008	0.756
		c-IMT $_{max}$	0.015	0.017	0.378	-0.002	0.016	0.894
		c-IMT $_{mean-max}$	0.016	0.01	0.092	0.005	0.009	0.575
		ICCAD	0.005	0.005	0.254	0	0.004	0.958
IV	741	c-IMT $_{mean}$	0.024	0.01	0.015	0.016	0.009	0.077
		c-IMT $_{max}$	0.051	0.018	0.004	0.039	0.016	0.018
		c-IMT $_{mean-max}$	0.031	0.01	0.003	0.022	0.009	0.021
		ICCAD	0.006	0.005	0.227	0.001	0.004	0.769

Abbreviations: *n* number of subjects. Model 1 univariate analysis
Model 2 adjusted for age, sex and population structure All c-IMT variables and ALT were logarithmically transformed before statistical analysis