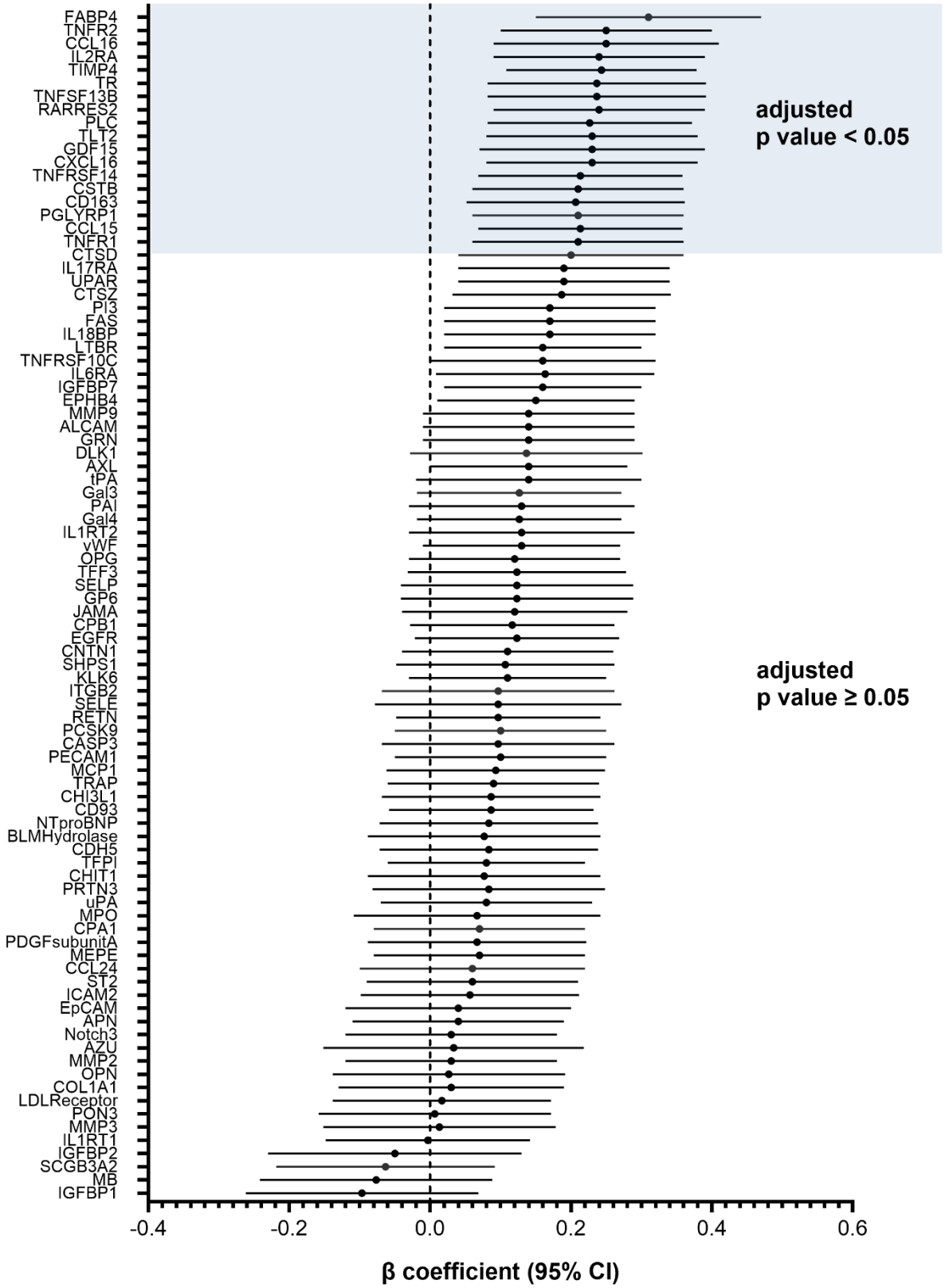
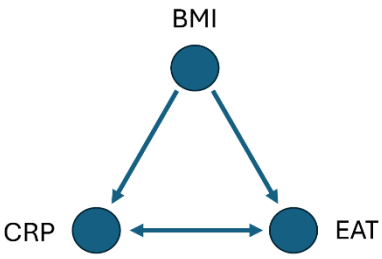
Supplementary Table 1. Sensitivity analysis of the association between biomarker and EAT with BMI adjustment. Linear mixed-effects models with EAT thickness as the dependent variable, adjusted for age, sex, bariatric surgery status, and BMI. Each model estimates the change in EAT (mm) per 1 SD increase in biomarker level. P-values were corrected for multiple testing using the Benjamini–Hochberg procedure to control the false discovery rate at 5%.

Biomarker	β-coefficient (95% CI)	Adjusted p-value	Biomarker	β-coefficient (95% CI)	Adjusted p-value
ALCAM	0.04 (0.02 - 0.06)	0.0006	LTBR	0.04 (0.02 - 0.06)	0.0006
APN	0.04 (0.02 - 0.06)	0.0006	MB	0.04 (0.02 - 0.07)	0.0006
AXL	0.04 (0.02 - 0.06)	0.0006	MCP1	0.04 (0.02 - 0.06)	0.0006
AZU	0.04 (0.02 - 0.07)	0.0006	MEPE	0.04 (0.02 - 0.06)	0.0006
BLMHydrolase	0.04 (0.02 - 0.06)	0.0006	MMP2	0.04 (0.02 - 0.06)	0.0006
CASP3	0.04 (0.02 - 0.07)	0.0006	MMP3	0.04 (0.02 - 0.06)	0.0006
CCL15	0.04 (0.02 - 0.06)	0.0006	MMP9	0.04 (0.02 - 0.06)	0.0001
CCL16	0.04 (0.01 - 0.06)	0.0002	MPO	0.04 (0.02 - 0.07)	0.0006
CCL24	0.04 (0.02 - 0.06)	0.0006	Notch3	0.04 (0.02 - 0.06)	0.0006
CD163	0.04 (0.01 - 0.06)	0.0018	NTproBNP	0.04 (0.02 - 0.06)	0.0006
CD93	0.04 (0.02 - 0.06)	0.0006	OPG	0.04 (0.02 - 0.06)	0.0006
CDH5	0.04 (0.02 - 0.06)	0.0006	OPN	0.04 (0.02 - 0.06)	0.0006
CHI3L1	0.04 (0.02 - 0.06)	0.0006	PAI	0.04 (0.02 - 0.06)	0.0007
CHIT1	0.04 (0.02 - 0.06)	0.0006	PCSK9	0.04 (0.02 - 0.06)	0.0006
CNTN1	0.04 (0.02 - 0.07)	0.0006	PDGFsubunitA	0.04 (0.02 - 0.06)	0.0006
COL1A1	0.04 (0.02 - 0.07)	0.0006	PECAM1	0.04 (0.02 - 0.06)	0.0006
CPA1	0.04 (0.02 - 0.06)	0.0006	PGLYRP1	0.04 (0.01 - 0.06)	0.0012
CPB1	0.04 (0.02 - 0.06)	0.0006	PI3	0.04 (0.02 - 0.06)	0.0008
CSTB	0.04 (0.01 - 0.06)	0.0002	PLC	0.03 (0.01 - 0.06)	0.0003
CTSD	0.04 (0.02 - 0.06)	0.0011	PON3	0.05 (0.02 - 0.07)	0.0006
CTSZ	0.04 (0.02 - 0.06)	0.0009	PRTN3	0.04 (0.02 - 0.06)	0.0006
CXCL16	0.04 (0.02 - 0.06)	0.0009	RARRES2	0.03 (0.01 - 0.06)	0.0034
DLK1	0.04 (0.02 - 0.06)	0.0006	RETN	0.04 (0.02 - 0.06)	0.0006
EGFR	0.04 (0.02 - 0.06)	0.0006	SCGB3A2	0.04 (0.02 - 0.06)	0.0006
EpCAM	0.04 (0.02 - 0.07)	0.0006	SELE	0.04 (0.02 - 0.06)	0.0006
EPHB4	0.04 (0.02 - 0.06)	0.0006	SELP	0.04 (0.02 - 0.06)	0.0006
FABP4	0.03 (0.00 - 0.05)	0.0304	SHPS1	0.04 (0.02 - 0.06)	0.0006
FAS	0.04 (0.02 - 0.06)	0.0008	ST2	0.04 (0.02 - 0.06)	0.0006
Gal3	0.04 (0.02 - 0.06)	0.0008	TFF3	0.04 (0.02 - 0.06)	0.0006
Gal4	0.04 (0.02 - 0.06)	0.0006	TFPI	0.04 (0.02 - 0.06)	0.0006
GDF15	0.04 (0.02 - 0.06)	0.0009	TIMP4	0.04 (0.02 - 0.06)	0.0009
GP6	0.04 (0.02 - 0.07)	0.0006	TLT2	0.04 (0.02 - 0.06)	0.0007
GRN	0.04 (0.02 - 0.06)	0.0007	TNFR1	0.04 (0.01 - 0.06)	0.0002
ICAM2	0.04 (0.02 - 0.06)	0.0006	TNFR2	0.04 (0.01 - 0.06)	0.0002
IGFBP1	0.04 (0.02 - 0.06)	0.0006	TNFRSF10C	0.04 (0.02 - 0.06)	0.0008
IGFBP2	0.04 (0.02 - 0.07)	0.0006	TNFRSF14	0.04 (0.02 - 0.06)	0.0006
IGFBP7	0.04 (0.02 - 0.06)	0.0006	TNFSF13B	0.04 (0.02 - 0.06)	0.0011
IL17RA	0.04 (0.02 - 0.06)	0.0006	tPA	0.04 (0.02 - 0.06)	0.0009
IL18BP	0.04 (0.02 - 0.06)	0.0006	TR	0.04 (0.02 - 0.06)	0.0008
IL1RT1	0.04 (0.02 - 0.06)	0.0006	TRAP	0.04 (0.02 - 0.06)	0.0006
IL1RT2	0.04 (0.02 - 0.06)	0.0006	uPA	0.04 (0.02 - 0.06)	0.0006
IL2RA	0.04 (0.01 - 0.06)	0.0013	UPAR	0.04 (0.02 - 0.06)	0.0012
IL6RA	0.04 (0.02 - 0.06)	0.0008	vWF	0.04 (0.02 - 0.06)	0.0007
ITGB2	0.04 (0.02 - 0.06)	0.0006			
JAMA	0.04 (0.02 - 0.07)	0.0006			
KLK6	0.04 (0.02 - 0.07)	0.0006			
LDLReceptor	0.04 (0.02 - 0.07)	0.0006			

Supplementary Figure 1 Forrest plot of linear mixed model of all analyzed biomarkers. Beta coefficient indicates increase in EAT (in mm) for each increase in 1 SD of biomarker level. The p value was corrected for multiple testing using the Benjamini–Hochberg procedure, with a 5% false discovery rate.



Supplementary Figure 2 Directed acyclic graph and simplified hypothetical example of the concept of negative confounding



Hypothetical data

	BMI	CRP	EAT
A	20	1	2
B	20	2	2.5
C	30	2	5
D	30	3	5.5

Within each BMI stratum, higher CRP is associated with higher EAT. Across the full dataset, individuals with similar CRP but different BMI show markedly different EAT. Because BMI strongly influences EAT and is correlated with CRP, this masks the overall CRP–EAT association, illustrating negative confounding.
BMI, body mass index; CRP, C-reactive protein; EAT, Epicardial adipose tissue