Appendix 1

Methods

1. Study design

1.1 Groups being compared

The study involved four groups of male C57BL/6 mice (4 weeks old): normal diet (ND) group: 6 mice fed a normal diet (10% kcal fat, Research diets D12450J) for 8 weeks. High fat diet (HFD) group: 6 mice fed a HFD (60% kcal fat, Research diets D12492) for 8 weeks. HFD-AngII group: 6 mice fed a HFD for 8 weeks, followed by implantation with osmotic minipumps containing human angiotensin II (AngII) (1,000 ng/min/kg, dissolved in saline, MedChemExpress) for an additional 4 weeks. ND-AngII group: 10 mice fed a normal diet for 8 weeks, followed by implantation with osmotic minipumps containing human AngII for an additional 4 weeks. Control groups: the ND groups serve as control groups to compare the effects of HFD feeding and AngII administration.

1.2 Experimental unit

The experimental unit in this study was a single mouse. Each mouse was individually housed and treated according to its assigned group.

1.3 Sample size determination

The sample size for this study was determined based on the number of animals used in previous literature with similar experimental setups (31,32). This ensures that the study is adequately powered to detect significant differences between the groups.

1.4 Inclusion and exclusion criteria

1.4.1 Criteria for including and excluding animals

Inclusion criteria: mice are healthy and free from any observable signs of disease and they have acclimated to the laboratory conditions for at least one week before starting the experiment.

Exclusion criteria: mice exhibit signs of illness or abnormal behavior during the experiment. If mice that fail to consume the provided diet or exhibit extreme weight loss (greater than 20% of body weight compared to their group average), they will be excluded. Any mouse experiences unforeseen complications or death during the experiment will be excluded from the final analysis.

1.4.2 Criteria for including and excluding data points during analysis

Inclusion criteria: data points collected from mice that met all inclusion criteria and completed the entire experimental protocol.

Exclusion criteria: data points from mice that were excluded based on the animal exclusion criteria. Data points are identified as outliers due to technical errors, such as equipment malfunction or human error during data collection. Data points that are missing or incomplete due to unforeseen circumstances.

There were no exclusions during animal experiments

1.5 Randomization

Mice were randomly assigned to one of the four groups using a computer-generated randomization sequence.

1.6 Strategies for minimising potential confounders

Mice were housed in identical conditions and their cages were rotated regularly within the animal facility to mitigate any potential location effects. Treatments and measurements were conducted in a random order to avoid any systematic biases. All handling and experimental procedures were performed by the same set of trained personnel to ensure consistency.

1.7 Blinding and group allocation awareness

During allocation: the person responsible for generating the randomisation sequence and assigning the mice to their respective groups was aware of the group allocations. This person was not involved in the subsequent conduct of the experiment, outcome assessment, or data analysis to ensure unbiased results.

During the conduct of the experiment: the researchers who conducted the daily care and feeding of the mice were aware of the group allocations to ensure that the correct diets and treatments were administered. However, these researchers were not involved in the outcome assessment or data analysis.

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During outcome assessment: the researchers conducting the outcome assessments, including measurements and observations, were blinded to the group allocations. This blinding helps to reduce bias in the collection of data and ensures objective assessment of the experimental outcomes.

During data analysis: the data analysts were also blinded to the group allocations during the data analysis phase. The data was coded to prevent any bias in the interpretation of the results. The blinding was maintained until the final statistical analysis was completed.

References

31. Cheng YW, Zhang ZB, Lan BD, et al. PDGF-D activation by macrophage-derived uPA promotes AngII-induced cardiac remodeling in obese mice. J Exp Med 2021;218:e20210252.
32. Withaar C, Meems LMG, Markousis-Mavrogenis G, et al. The effects of liraglutide and dapagliflozin on cardiac function and structure in a multi-hit mouse model of heart failure with preserved ejection fraction. Cardiovasc Res 2021;117:2108-24.

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Table S1 Clinical characteristics of subjects

Characteristics	All group (n=237)	AD (n=148)	IHM (n=42)	AA (n=47)
Gender (female/male)	40/197	18/130	10/32	12/35
Age (years)	55.64±14.13	52.82±13.83	58.88±12.95	61.62±13.88
BMI (kg/m^2)	25.60±3.92	26.14±3.84	25.04±3.87	24.42±3.93
BMI <24	82 (34.6)	45 (30.4)	16 (38.1)	21 (44.7)
24≤ BMI <28	91 (38.4)	60 (40.5)	15 (35.7)	16 (34.0)
BMI ≥28	60 (25.3)	40 (27.0)	11 (26.2)	9 (19.2)
Hypertension	133 (56.1)	87 (58.8)	30 (71.4)	16 (34.0)
Diabetes	17 (7.2)	7 (4.7)	4 (9.5)	6 (12.8)
Smokers	74 (31.2)	53 (35.8)	13 (31.0)	8 (17.0)
Drinkers	49 (20.7)	29 (19.6)	10 (23.8)	10 (21.3)
Death	16 (6.8)	9 (6.1)	7 (16.7)	0 (0.0)
Postoperative hospital stay (days)	23.16±11.34	26.11±12.94	16.86±8.66	19.71±9.07

Data are shown as mean ± standard deviation, number, or number (percentage). Three patients in AD group and one patient in AA group missed BMI data. AD, aortic dissection; IHM, intramural hematoma; AA, aortic aneurysm; BMI, body mass index.

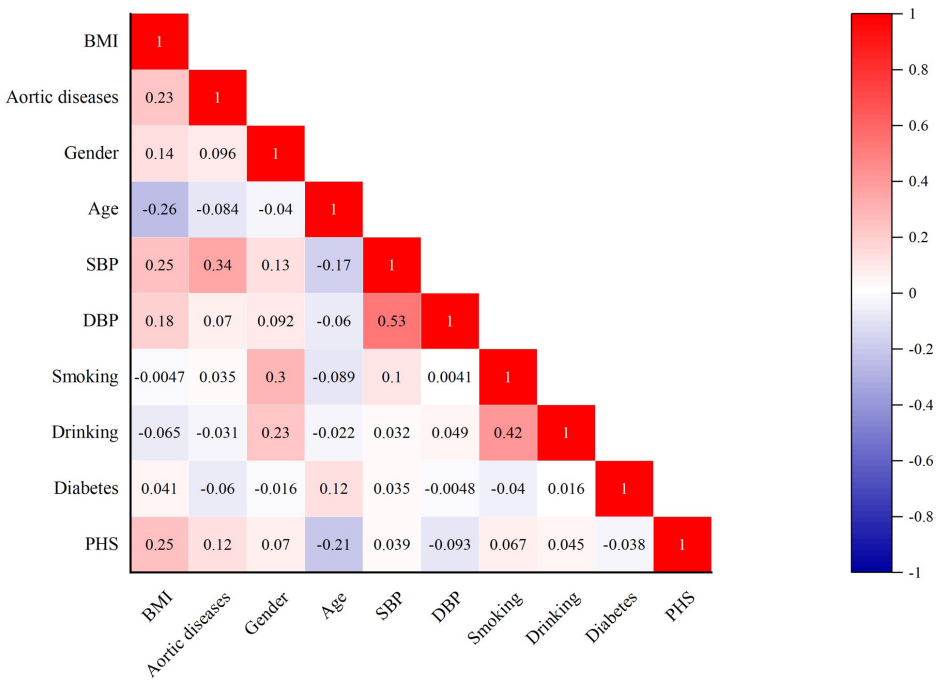

Figure S1 The correlation of general characteristics in patients with aortic disease. Positive correlations are indicated in red, while negative correlations are shown in blue. The intensity of the color reflects the strength of the correlation coefficients. The coefficients of the variables displayed are statistically significant (BMI; aortic disease; gender; age; SBP; DBP; smoking; drinking; diabetes; PHS). BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; PHS, postoperative hospital stay.

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Table S2 BMI-associations with clinical characteristics

Characteristics	Normal BMI (n=82)	Overweight (n=90)	Obesity (n=60)	χ^2/F/H	P
Diabetes	5 (6.1)	7 (7.8)	5 (8.3)	0.299	0.86
Smokers	27 (32.9)	29 (32.2)	17 (28.3)	0.378	0.82
Drinkers	18 (22.0)	19 (21.1)	12 (20.0)	0.079	0.96
Death	4 (4.9)	6 (6.7)	4 (6.7)	0.299	0.86
PLT (10^9/L)	166.000 (118.0, 194.3)	174.000 (135.5, 205.3)	183.000 (142.3, 217.5)	3.453	0.17
LYM (10^9/L)	0.875 (0.7, 1.4)	0.990 (0.6, 1.3)	1.080 (0.8, 1.6)	4.568	0.10
DD (μg/mL)	1.820 (0.8, 6.4)	3.660 (0.9, 13.6)	2.890 (0.6, 11.0)	4.113	0.12
CRP (mg/L)	7.780 (2.9, 16.4)	13.210 (4.6, 24.5)	12.350 (3.7, 25.6)	4.673	0.09
TP (g/L)	61.900 (58.5, 65.9)	62.750 (58.0, 65.7)	63.100 (58.3, 67.7)	1.959	0.37
PA (mg/L)	213.20±53.48	228.27±68.46	236.92±65.20	2.661	0.07
GLU (mmol/L)	6.355 (4.9, 7.8)	6.915 (5.8, 8.0)	6.850 (5.7, 8.3)	4.178	0.12
TC (mmol/L)	4.000 (3.5, 4.6)	4.180 (3.6, 4.9)	4.195 (3.6, 5.0)	2.247	0.32
LDL-C (mmol/L)	2.315 (1.7, 2.8)	2.425 (1.9, 3.2)	2.615 (2.1, 3.0)	3.761	0.15
HsTnT (pg/mL)	12.490 (7.7, 27.2)	13.210 (7.4, 25.5)	10.890 (7.8, 23.0)	0.157	0.92
MB (ng/mL)	41.300 (27.5, 87.3)	43.650 (27.6, 109.8)	44.290 (27.2, 104.3)	0.144	0.93
CK-MB (ng/mL)	1.590 (0.9, 2.8)	1.530 (0.9, 2.5)	1.760 (1.1, 3.6)	1.892	0.38
TBIL (μmol/L)	14.150 (11.4, 20.4)	16.200 (12.4, 22.7)	16.200 (12.6, 23.6)	3.369	0.18
DBIL (μmol/L)	5.050 (4.1, 6.9)	5.400 (4.3, 8.4)	5.850 (4.1, 8.1)	2.3	0.31
IBIL (μmol/L)	9.250 (7.5, 13.1)	10.700 (8.1, 14.5)	10.850 (8.4, 15.1)	3.427	0.18
ALT (U/L)	19.500 (12.2, 29.3)	21.150 (12.9, 34.9)	24.950 (16.6, 42.3)	7.236	0.26
AST (U/L)	20.600 (15.3, 29.2)	20.600 (15.4, 28.1)	20.450 (15.9, 27.3)	0.169	0.91
BUN (mmol/L)	6.700 (4.9, 8.6)	6.950 (5.2, 9.6)	7.450 (5.5, 9.6)	2.36	0.30
Cre (μmol/L)	71.100 (58.1, 93.0)	85.650 (68.6, 104.4)	87.050 (63.8, 110.0)	10.321	0.36
CysC (mg/L)	1.010 (0.9, 1.3)	1.080 (0.9, 1.3)	1.000 (0.9, 1.2)	2.508	0.28

F means using Fisher exact test. H means using Kruskal-Wallis H Test. BMI, body mass index; PLT, platelet; LYM, lymphocyte; DD, D-dimer; CRP, C-reactive protein; TP, total protein; ALB, albumin; PA, prealbumin; GLU, glucose; HbA1C, glycosylated hemoglobin; TC, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HsTnT, high sensitive troponin T; MB, myoglobin; CK-MB, creatine kinase-MB; TBIL, total bilirubin; DBIL, direct bilirubin; IBIL, indirect bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cre, creatinine; CysC, cystatin C.

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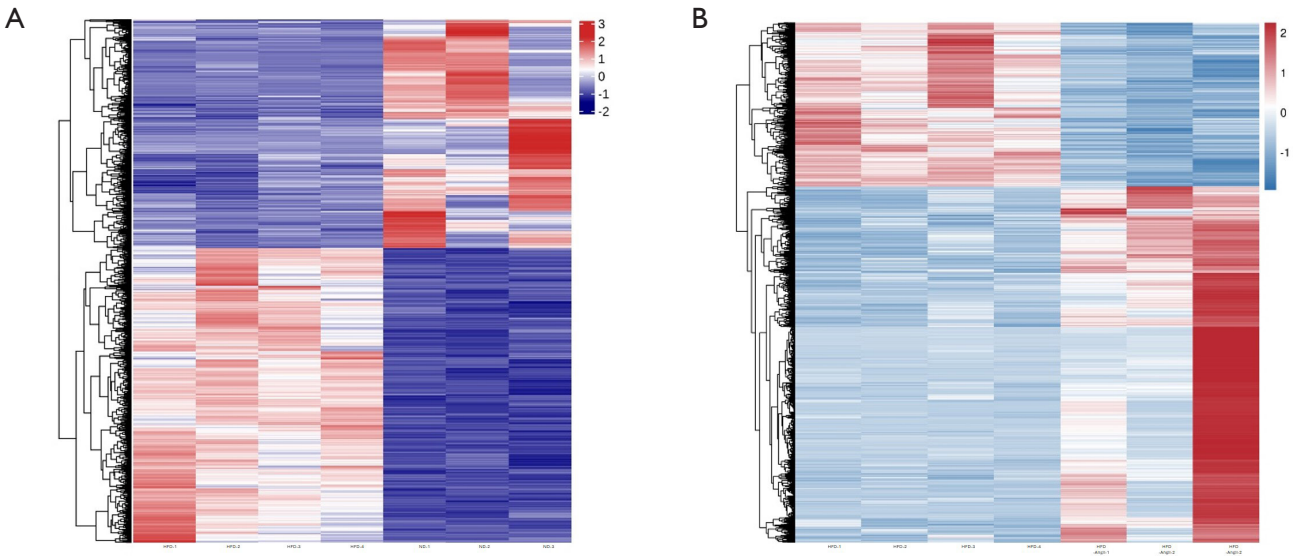

Figure S2 Heatmaps of gene expression profiles among the three different groups. (A) DEGs in ND *vs.* HFD. (B) DEGs in HFD *vs.* HFD-AngII. Color bars [red to blue (3 to –2) vertical bars] represent the value of row-scaled log2 transformed gene expression from microarray. HFD, high fat diet; ND, normal diet; DEGs, differentially expressed genes.

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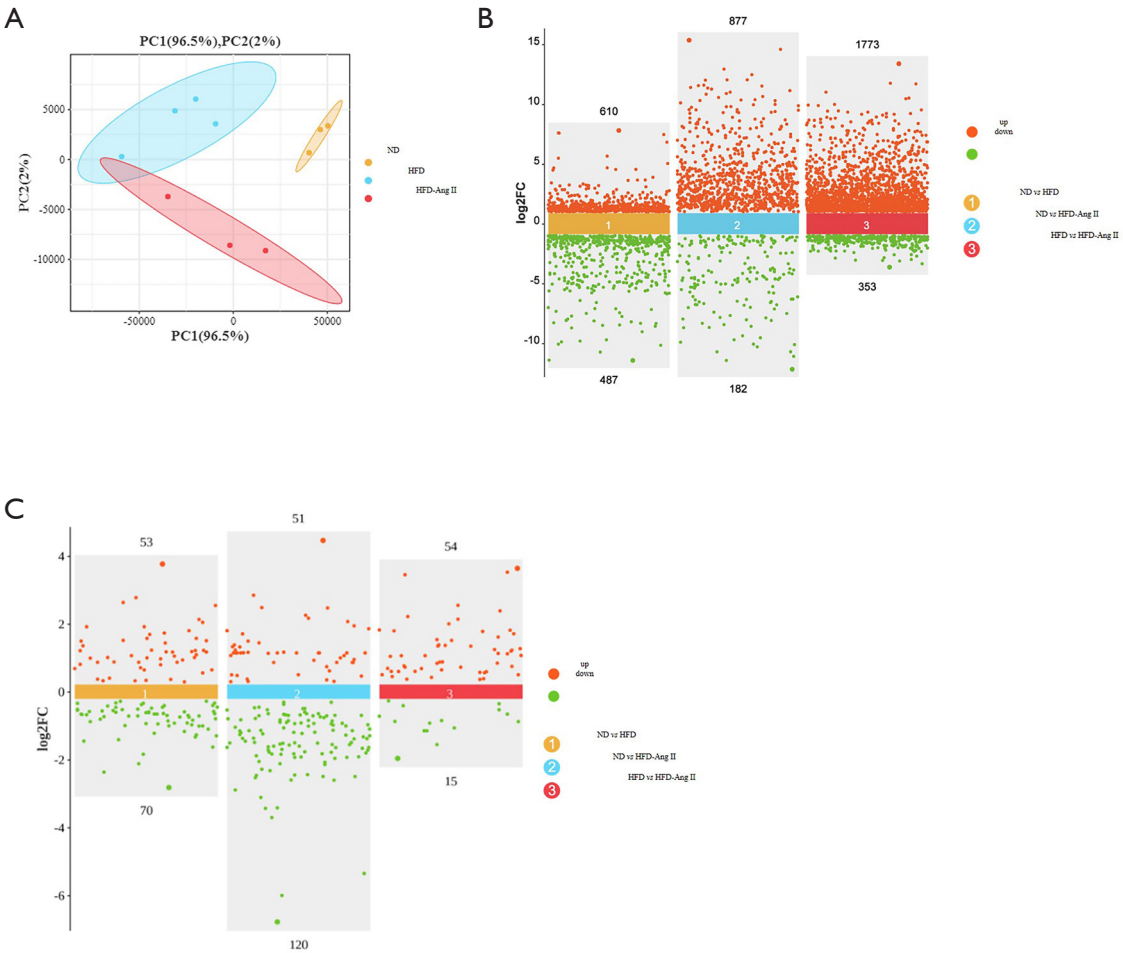

Figure S3 Changes in gene and protein expression among the three different groups. (A) PCA of three groups. (B) The number of up-regulated and down-regulated genes between groups (|log2 FC| >1, P values <0.05). (C) Scatterplot of up-regulated and down-regulated proteins with differential expression between groups (FC >1.2 or FC <0.833, P value <0.05). HFD, high fat diet; ND, normal diet; FC, fold change; PCA, principal component analysis.

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Table S3 Genes in common pathways

Pathway	Transcriptomics profile 0	Transcriptomics profile 7
Complement and coagulation cascades	Fgg; C9; C4bpa; C5; F13b	Itgam; C1sa; F13a1; C5ar1; C1qa; C1qc; Serping1; C1qb; C3; C4b; C1ra
Prion disease	C9; C5	Ncam2; Prnp; Il6; C1qa; C1qc; C1qb

Table S4 Protein in common pathways

Pathway	Protein profile 0	Protein profile 7
African trypanosomiasis	Hba	Apoa1
Estrogen signaling pathway	Egfr; Mmp2	Krt18

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