Supplemental material

Table S1. Characteristics of the study population at baseline, by sex

Characteristic	Men (*n*=960)	Women (*n*=1143)	*p*-value
Age, y	68 (6.20)	68 (6.44)	0.948
Waist, cm	98.7 (9.92)	89.5 (10.9)	<0.001
BMI, kg/m^2	27.4 (3.32)	27.9 (4.40)	0.004
SBP, mmHg	146 (19.4)	147 (20.3)	0.401
DBP, mmHg	82.0 (10.8)	79.4 (10.6)	<0.001
Anti-hypertensive medication use, *n* (%)	335 (35.5)	410 (36.2)	0.778
Smoking , *n* (%)			<0.001
Current	175 (18.8)	154 (13.7)	
Never	142 (15.2)	467 (41.6)	
Former	616 (66.0)	501 (44.7)	
Total cholesterol, mmol/l	5.48 (0.91)	5.97 (0.94)	<0.001
HDL cholesterol, mmol/l	1.32 (0.34)	1.57 (0.40)	<0.001
Lipid lowering medication use, *n* (%)	189 (19.7)	254 (22.1)	0.185
Prevalent DM, *n* (%)	118 (12.3)	133 (11.6)	0.672
EFV, ml	122.2 (39.9)	91.7 (28.9)	<0.001
Echocardiographic parameters			
LVEDD, mm	53.8 (4.48)	50.2 (4.27)	<0.001
LVESD, mm	32.4 (4.54)	29.4 (4.04)	<0.001

LVEF, %	64.5 (7.02)	66.7 (6.20)	<0.001
LA diameter, mm	41.8 (5.18)	38.9 (5.00)	<0.001
E/A ratio	0.93 (0.24)	0.89 (0.29)	0.001
DT, ms	215.8 (44.7)	209.5 (40.7)	<0.001

Data are mean (SD) for continuous variables and numbers (percentages) for categorical variables.

BMI; Body Mass Index, SBP; systolic blood pressure, DBP; diastolic blood pressure, HDL; high-density lipoprotein; DM; diabetes mellitus, CHD; coronary heart disease, EFV; epicardial fat volume, LVEDD; left ventricular end diastolic dimension, LVESD; left ventricular end systolic dimension, LVEF; left ventricular ejection fraction, LA diameter; left atrial anteroposterior dimension, E/A ratio; E-wave to A-wave ration, DT; Deceleration time

Table S 2. Association of epicaridal fat volume with repeated measures of echocardiographic parameters of cardiac function in total population, including the time interaction term

		Model 1		Model 2	
Echocardiographic parameters		**β (95% CI)**	***p*-value**	**β (95% CI)**	***p*-value**
LVEDD	EFV	1.28 (1.08 to 1.49)	<0.001	0.76 (0.53 to 0.99)	<0.001
	EFV:time	-0.004 (-0.03 to 0.02)	0.762	-0.001 (-0.03 to 0.02)	0.916
LVESD	EFV	1.10 (0.92 to 1.28)	<0.001	0.73 (0.52 to 0.94)	<0.001
	EFV:time	-0.02 (-0.04 to 0.01)	0.132	-0.02 (-0.04 to 0.003)	0.088
LVEF	EFV	-0.77 (-1.07 to -0.47)	<0.001	-0.59 (-0.92 to -0.25)	0.001
	EFV:time	-0.0001 (-0.04 to 0.04)	0.995	0.01 (-0.03 to 0.05)	0.758
LA diameter	EFV	1.65 (1.42 to 1.88)	<0.001	0.85 (0.59 to 1.11)	<0.001
	EFV:time	0.06 (0.03 to 0.09)	<0.001	0.05 (0.03 to 0.08)	<0.001
E/A ratio	EFV	-0.01 (-0.02 to -0.004)	0.006	-0.003 (-0.02 to 0.01)	0.558
	EFV:time	0.001 (-0.0001 to 0.002)	0.053	0.001 (0 to 0.002)	0.067
DT	EFV	1.21 (-0.68 to 3.10)	0.210	0.50 (-1.66 to 2.66)	0.650
	EFV:time	-0.25 (-0.53 to 0.03)	0.081	-0.13 (-0.41 to 0.15)	0.365

Results are based on linear mixed effects models. Model 1 is adjusted for age (time-varying), sex and cohort. Model 2 is additionally adjusted baseline values of prevalent diabetes, body mass index, smoking, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medication, total

and high-density lipoprotein (HDL) cholesterol, use of lipid lowering medication and interaction between EFV and time (EFV:time)

LVEDD; left ventricular end diastolic dimension, LVESD; left ventricular end systolic dimension, LVEF; left ventricular ejection fraction, LA diameter; left atrial anteroposterior dimension, E/A ratio; E-wave to A-wave ration, DT; Deceleration time

The number of men with available data on outcomes was 2065 for LVEDD, 2037 for LVESD, 2045 for LVEF, 2089 for LA diameter, 2074 for E/A ratio and 2045 for DT

Table S3. Association of epicaridal fat volume with repeated measures of echocardiographic parameters of cardiac function, by sex

	Men		Women	
Echocardiographic parameters	**β (95% CI)**	***p*-value**	**β (95% CI)**	***p*-value**
LVEDD	0.47 (0.16 to 0.77)	0.003	1.18 (0.85 to 1.51)	<0.001
LVESD	0.44 (0.16 to 0.73)	0.003	0.95 (0.68 to 1.22)	<0.001
LVEF	-0.66 (-1.11 to -0.21)	0.004	-0.42 (-0.83 to -0.001)	0.049
LA diameter	0.89 (0.56 to 1.22)	<0.001	1.15 (0.76 to 1.54)	<0.001
E/A ratio	-0.001 (-0.02 to 0.01)	0.898	0.004 (-0.01 to 0.02)	0.670
DT	-0.96 (-3.69 to 1.77)	0.490	1.435 (-1.48 to 4.35)	0.335

Results are based on linear mixed effects models. Models are adjusted for age(time-varying), sex, cohort, and baseline values of prevalent diabetes, body mass index, smoking, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medication, total and high-density lipoprotein (HDL) cholesterol, use of lipid lowering medication

LVEDD; left ventricular end diastolic dimension, LVESD; left ventricular end systolic dimension, LVEF; left ventricular ejection fraction, LA diameter; left atrial anteroposterior dimension, E/A ratio; E-wave to A-wave ration, DT; Deceleration time

The number of men with available data on outcomes was 939 for LVEDD, 921 for LVESD, 925 for LVEF, 951 for LA diameter, 945 for E/A ratio and 927 for DT

The number of men with available data on outcomes was 1126 for LVEDD, 1116 for LVESD, 1120 for LVEF, 1139 for LA diameter, 1129 for E/A ratio and 1118 for DT

Table S4. Association of epicaridal fat volume with repeated measures of echocardiographic parameters of cardiac function, including the time interaction term by sex

		Men		Women	
Echocardiographic parameters		**β (95% CI)**	***p*-value**	**β (95% CI)**	***p*-value**
LVEDD	EFV	0.40 (0.07 to 0.72)	0.017	1.317 (0.96 to 1.68)	<0.001
	EFV:time	0.02 (-0.01 to 0.06)	0.219	-0.04 (-0.08 to 0.002)	0.061
LVESD	EFV	0.46 (0.15 to 0.77)	0.004	1.11 (0.80 to 1.41)	<0.001
	EFV:time	-0.01 (-0.04 to 0.03)	0.802	-0.04 (-0.07 to -0.01)	0.025
LVEF	EFV	-0.65 (-1.13 to -0.16)	0.009	-0.59 (-1.10 to -0.07)	0.027
	EFV:time	-0.004 (-0.07 to 0.06)	0.893	0.04 (-0.03 to 0.10)	0.281
LA diameter	EFV	0.71 (0.36 to 1.07)	<0.001	0.89 (0.47 to 1.32)	<0.001
	EFV:time	0.06 (0.02 to 0.10)	0.006	0.07 (0.03 to 0.12)	0.003
E/A ratio	EFV	-0.01 (-0.02 to 0.01)	0.412	-0.003 (-0.02 to 0.01)	0.726
	EFV:time	0.002 (0 to 0.004)	0.077	0.002 (-0.0001 to 0.01)	0.055
DT	EFV	0.15 (-2.93 to 3.22)	0.926	1.57 (-1.83 to 4.98)	0.365
	EFV:time	-0.32 (-0.73 to 0.09)	0.125	-0.04 (-0.50 to 0.43)	0.878

Results are based on linear mixed effects models. Models are adjusted for age (time-varying), sex, cohort, and baseline values of prevalent diabetes, body mass index, smoking, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medication, total and high-density

lipoprotein (HDL) cholesterol, use of lipid lowering medication and interaction between EFV and time (EFV:time)

LVEDD; left ventricular end diastolic dimension, LVESD; left ventricular end systolic dimension, LVEF; left ventricular ejection fraction, LA diameter; left atrial anteroposterior dimension, E/A ratio; E-wave to A-wave ration, DT; Deceleration time

The number of men with available data on outcomes was 939 for LVEDD, 921 for LVESD, 925 for LVEF, 951 for LA diameter, 945 for E/A ratio and 927 for DT

The number of men with available data on outcomes was 1126 for LVEDD, 1116 for LVESD, 1120 for LVEF, 1139 for LA diameter, 1129 for E/A ratio and 1118 for DT

Table S5. Association of EFV with incident heart failure, by sex

	Men		Women	
	HR (95% CI)*	***p*-value**	**HR (95% CI)***	***p*-value**
Model 1	1.39 (1.11 to 1.76)	0.010	1.38 (1.03 to1.84)	0.030
Model 2	1.30 (0.97 to 1.76)	0.080	1.36 (0.96 to 1.93)	0.088
Model 3[†]	1.34 (1.00 to 1.82)	0.053	1.27 (0.80 to 2.02)	0.312
Model 4[‡]	1.30 (0.97 to 1.74)	0.079	1.36 (0.85 to 2.17)	0.204

Model 1 is adjusted for age, sex and cohort. Model 2 is additionally adjusted for prevalent diabetes, body mass index, smoking, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medication, total and high-density lipoprotein (HDL) cholesterol, use of lipid lowering medication. Model 3 is model 2 + additionally adjusted for CHD as a time varying covariate. Model 4 is model 2 + additionally adjusted for AF as a time varying covariate. EFV; epicardial fat volume AF; atrial fibrillation, CHD; coronary heart disease

*HR: Hazard ratio 95% CI: 95 % confidence interval

Table S6. Association of epicaridal fat volume with repeated measures of echocardiographic parameters of cardiac function in the total population, additionally adjusted for LVM index

Echocardiographic parameters	β (95% CI)	*p*-value
LVEDD	0.50 (0.32 to 0.67)	<0.001
LVESD	0.47 (0.30 to 0.64)	<0.001
LVEF	-0.45 (-0.74 to -0.16)	0.003
LA diameter	0.99 (0.75 to 1.23)	<0.001
E/A ratio	0.001 (-0.01 to 0.01)	0.972
DT	0.44 (-1.69 to 2.57)	0.686

Results are based on linear mixed effects models. Models are adjusted for age (time-varying), sex, cohort, and baseline values of prevalent diabetes, body mass index, smoking, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medication, total and high-density lipoprotein (HDL) cholesterol, use of lipid lowering medication and LVM

LVEDD; left ventricular end diastolic dimension, LVESD; left ventricular end systolic dimension, LVEF; left ventricular ejection fraction, LA diameter; left atrial anteroposterior dimension, E/A ratio; E-wave to A-wave ration, DT; Deceleration time; LVM: Left ventricular mass index by body surface area

Table S7. Association of epicardial fat volume with incident heart failure in the total population, additionally adjusted for LVM idex

	HR (95% CI)*	*p*-value
Model 2 + LVM index	1.29 (1.01 to 1.65)	0.043
Model 2 + LA diameter	1.28 (0.99 to 1.64)	0.056
Model 2 + LA diameter + LVM index	1.27 (0.99 to 1.62)	0.053

Model 2 is adjusted for age, sex, cohort, prevalent diabetes, body mass index, smoking, systolic blood pressure, diastolic blood pressure, use of anti-hypertensive medication, total and high-density lipoprotein (HDL) cholesterol, use of lipid lowering medication. LA diameter: left atrial diameter; LVM: Left ventricular mass index by body surface area

*HR: Hazard ratio 95% CI: 95 % confidence interval