Supplementary Information: Relations of Biomarkers of Extracellular Matrix Remodeling to Incident Cardiovascular Events and Mortality

Definitions of Covariates

We defined all covariates at examination cycle 6, which served as the baseline for the present investigation. We calculated body mass index (BMI) as the weight in kilograms divided by the square of height in meters. A physician measured blood pressure twice during the Heart Study clinic visit on the left arm of seated participants using a mercury-column sphygmomanometer and a cuff of appropriate size; we used the average of these two readings as the examination blood pressure. We defined diabetes as fasting plasma glucose of 126 mg/dl or greater, or the use of insulin or other hypoglycemic therapy. We defined “current smoking” as smoking on average at least one cigarette per day in the year preceding the baseline examination.

Supplementary Table I. Relations of ECM biomarkers to CVD and mortality – Referent Group

	CVD		Death	
	Adjusted HR (CI)	***P*-value**	**Adjusted HR (CI)**	***P*-value**
A. MMP-9 as binary covariate (n = 271; 12 CVD events and 9 deaths) *				
Age- and sex-adjusted	3.52 (1.03 – 12.10)	0.045	0.0 (0.0)	0.99
Multivariable-adjusted	4.29 (1.02 – 18.00)	0.047	0.0 (0.0)	0.99
B. log-TIMP-1 (n = 572; 26 CVD events and 17 deaths) †				
Age- and sex-adjusted	1.10 (0.72 – 1.69)	0.65	2.52 (1.49 – 4.27)	0.0006
Multivariable-adjusted	1.09 (0.75 – 1.60)	0.64	2.33 (1.35 – 4.00)	0.002
C. log-PIIINP (n = 512; 24 CVD events and 15 deaths) †				
Age- and sex-adjusted	1.09 (0.73 – 1.64)	0.67	1.54 (1.04 – 2.27)	0.03
Multivariable-adjusted	1.06 (0.68 – 1.66)	0.81	1.56 (1.02 – 2.37)	0.04

Multivariable model included age, sex, BMI, systolic blood pressure, hypertension treatment, diabetes, total cholesterol/high density lipoprotein cholesterol ratio, current smoking and LV mass (continuous variable).

* HR indicates hazards in those with detectable MMP-9 compared to those without.
† HR per standard deviation change in biomarker levels.

Supplementary Table II. Relations of ECM biomarkers to CVD and mortality – Remodeled Group

	CVD		Death	
	Adjusted HR (CI)	***P*-value**	**Adjusted HR (CI)**	***P*-value**
A. MMP-9 as binary covariate (n = 335; 52 CVD events and 32 deaths) *				
Age- and sex-adjusted	1.13 (0.61 – 2.09)	0.71	1.42 (0.67 – 2.98)	0.84
Multivariable-adjusted	0.95 (0.50 – 1.80)	0.87	1.10 (0.50 – 2.38)	0.82
B. log-TIMP-1 (n = 350; 55 CVD events and 34 deaths) †				
Age- and sex-adjusted	1.38 (1.07 – 1.77)	0.01	1.73 (1.29 – 2.32)	0.0003
Multivariable-adjusted	1.11 (0.84 – 1.47)	0.45	1.64 (1.16 – 2.30)	0.005
C. log-PIIINP (n = 323; 50 CVD events and 31 deaths) †				
Age- and sex-adjusted	1.52 (1.16 – 1.99)	0.003	1.50 (1.01 – 2.23)	0.04
Multivariable-adjusted	1.50 (1.09 – 2.06)	0.01	1.80 (1.23 – 2.70)	0.003

Multivariable model included age, sex, BMI, systolic blood pressure, hypertension treatment, diabetes, total cholesterol/high density lipoprotein cholesterol ratio, current smoking and LV mass (continuous variable).

* HR indicates hazards in those with detectable MMP-9 compared to those without.
† HR per standard deviation change in biomarker levels.