

Supplemental Material

Table S1. Univariate association of individual biomarkers with heart failure outcomes.

Biomarkers	HF hospitalization or elevated NTproBNP during follow-up or initiation of loop diuretics or CV death		HF hospitalization or CV death	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Biomarker (continuous)				
log2 (hsTnl)	1.18 (1.15, 1.21)	<.0001	1.30 (1.26, 1.35)	<.0001
log2 (NTproBNP)	1.40 (1.35, 1.46)	<.0001	1.80 (1.70, 1.90)	<.0001
log2 (GDF15)	1.67 (1.55, 1.80)	<.0001	2.08 (1.89, 2.29)	<.0001
log2 (GAL3)	1.94 (1.74, 2.16)	<.0001	2.36 (2.07, 2.69)	<.0001
log2 (ADPN)	1.53 (1.42, 1.66)	<.0001	1.90 (1.70, 2.12)	<.0001
Biomarkers (by cut-offs)				
Elevated hsTnl	1.77 (1.52, 2.06)	<.0001	2.76 (2.25, 3.39)	<.0001
Elevated NTproBNP	2.61 (2.27, 3.00)	<.0001	6.02 (4.84, 7.49)	<.0001
Elevated GDF15	2.09 (1.81, 2.40)	<.0001	3.02 (2.47, 3.69)	<.0001
Elevated GAL3	1.96 (1.70, 2.26)	<.0001	2.75 (2.25, 3.36)	0.0012
Elevated ADPN	1.92 (1.66, 2.22)	<.0001	2.93 (2.39, 3.58)	0.0002

ADPN: adiponectin; Gal-3: galectin-3; GDF-15: growth-differentiation-factor -15; hs-CRP: high sensitivity C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Table S2. Multivariable clinical predictors for the composite of heart failure hospitalization or cardiovascular death.

Variable	Hazard ratio(95%CI)	Wald X²	P value
Heart failure	2.89 (2.33, 3.58)	94.3	<.0001
eGFR (ml/min/1.73m ²)	0.98 (0.97, 0.98)	50.9	<.0001
Myocardial infarction	3.43 (2.00, 5.88)	20.1	<.0001
Duration of diabetes	1.02 (1.01, 1.03)	10.5	0.0012
age	1.01 (1.00, 1.03)	5.1	0.0244
Systolic BP (mmHg)	0.99 (0.99, 1.00)	3.8	0.0515
Hyperlipidemia	1.23 (0.96, 1.57)	2.7	0.0985
Hypertension	1.33 (0.93, 1.90)	2.4	0.1246
Male	0.91 (0.73, 1.13)	0.7	0.3933
Smoking Status	1.16 (0.83, 1.62)	0.7	0.3965

eGFR: estimate glomerular filtration rate; BP blood pressure.

Table S3. Multivariable clinical variables and biomarkers for the outcome of heart failure hospitalization and cardiovascular death.

Variable	Hazard ratio(95%CI)	Wald X ²	P value
log ₂ (NTproBNP)	1.45 (1.34, 1.57)	78.8	<.0001
Heart Failure	2.20 (1.76, 2.76)	47.2	<.0001
log ₂ (hsTnl)	1.10 (1.04, 1.16)	12.0	0.0005
log ₂ (GDF15)	1.22 (1.05, 1.41)	7.0	0.0080
Hyperlipidemia	1.41 (1.08, 1.83)	6.6	0.0103
Hypertension	1.54 (1.07, 2.23)	5.3	0.0216
Myocardial infarction	1.85 (1.06, 3.23)	4.7	0.0302
Duration of diabetes	1.01 (1.00, 1.02)	2.9	0.0873
log ₂ (GAL3)	1.18 (0.95, 1.47)	2.2	0.1411
Systolic BP (mmHg)	1.00 (0.99, 1.00)	1.6	0.2122
Age	1.01 (1.00, 1.02)	1.3	0.2516
Male	0.90 (0.71, 1.13)	0.8	0.3642
Smoking Status	1.16 (0.82, 1.63)	0.7	0.3959
log ₂ (ADPN)	1.03 (0.90, 1.17)	0.2	0.6861
eGFR (ml/min/1.73m ²)	1.00 (0.99, 1.01)	0.04	0.8306

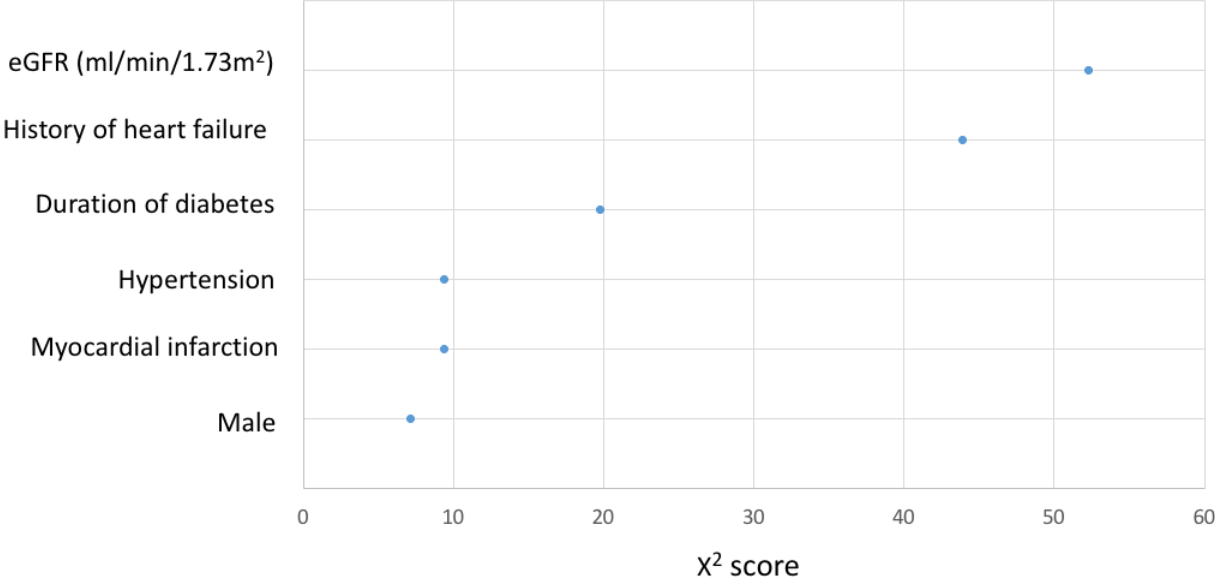
ADPN: adiponectin; Gal-3: galectin-3; GDF-15: growth-differentiation-factor -15; eGFR estimated glomerular filtration rate; hs-CRP: high sensitivity C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Table S4. Discrimination for the outcome of heart failure hospitalization or cardiovascular death.

Models	c-statistic	Change in c-statistic	Continuous NRI (95% Bootstrap CI)	IDI (95% Bootstrap CI)
Clinical model*	0.75			
Clinical model + hsTnI	0.78	0.036	0.5778 (0.4562, 0.6992)	0.0708 (0.0527, 0.0921)
Clinical model + NTproBNP	0.82	0.075	0.6684 (0.5655, 0.7735)	0.1619 (0.1344, 0.1947)
Clinical model + GDF15	0.76	0.016	0.2066 (0.0818, 0.3356)	0.0305 (0.0181, 0.046)
Clinical model + GAL3	0.76	0.011	0.2246 (0.1062, 0.3401)	0.0208 (0.0123, 0.0311)
Clinical model + ADPN	0.76	0.015	0.2644 (0.1422, 0.3887)	0.0132 (0.0037, 0.0236)
Clinical model + All biomarkers	0.83	0.082	0.6994 (0.5924, 0.8101)	0.1747 (0.145, 0.2091)
Clinical model + hsTnI (by cut-offs)	0.76	0.016	0.4460 (0.3213, 0.5796)	0.0411 (0.0276, 0.0553)
Clinical model + NTproBNP (by cut-offs)	0.81	0.060	0.9041 (0.7951, 1.0132)	0.1302 (0.1099, 0.1516)
Clinical model + GDF15 (by cut-offs)	0.76	0.010	0.4195 (0.3013, 0.5416)	0.0168 (0.0094, 0.0239)
Clinical model + GAL3 (by cut-offs)	0.76	0.007	0.3139 (0.1853, 0.4307)	0.0131 (0.0081, 0.019)
Clinical model + ADPN (by cut-offs)	0.76	0.014	0.4065 (0.2829, 0.5394)	0.0198 (0.0105, 0.0295)
Clinical model + All biomarkers (by cut-offs)	0.82	0.068	0.8276 (0.721, 0.9346)	0.1522 (0.1299, 0.1791)

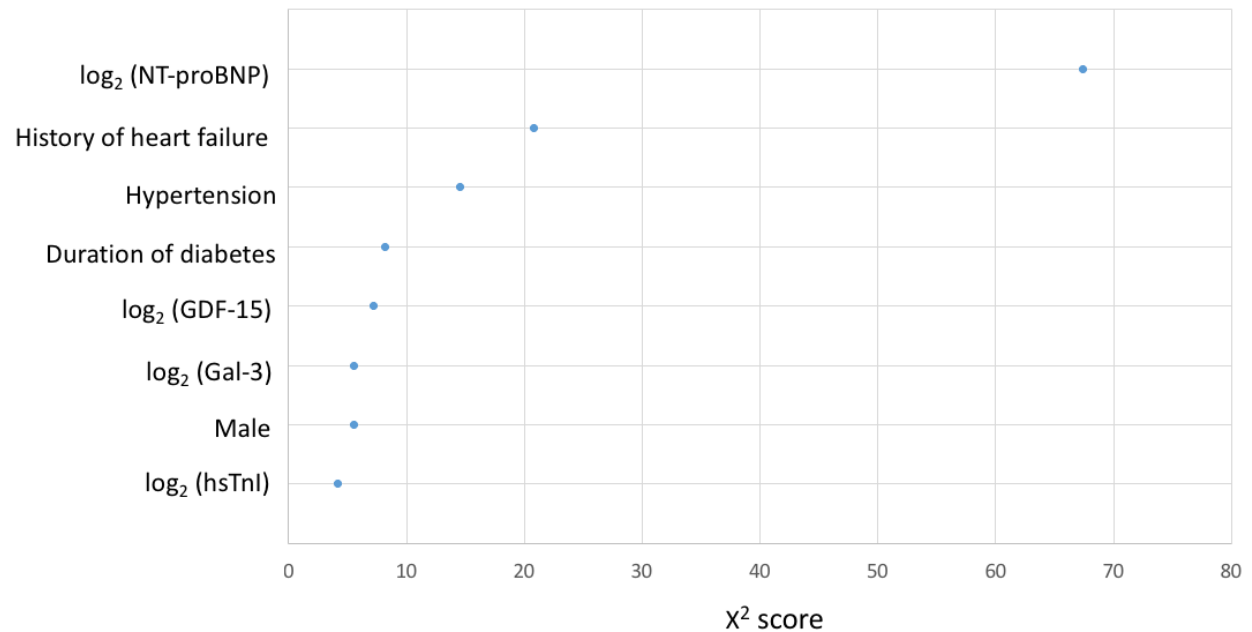
*The clinical model adjusted by age (continuous), sex, systolic blood pressure (continuous), history of heart failure, duration of diabetes, prior myocardial infarction, hypertension, hyperlipidemia, smoking, estimated glomerular filtration rate (continuous). ADPN: adiponectin; Gal-3: galectin-3; GDF-15: growth-differentiation-factor -15; hs-CRP: high sensitivity C-reactive protein; NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Figure S1. Relative importance of clinical variables for the composite outcome of cardiovascular death, heart failure hospitalization, initiation of loop diuretics, or elevated NT-proBNP during follow-up.



eGFR estimated glomerular filtration rate. Variables with a p-value ≥ 0.05 for the association with the variable and outcome in multivariable analysis are not displayed. A higher X² score implies a stronger association with the outcome.

Figure S2. Relative importance of clinical variables and biomarkers for the composite outcome of cardiovascular death, heart failure hospitalization, initiation of loop diuretics, or elevated NT-proBNP during follow-up.



NT-proBNP N-terminal pro-B-type natriuretic peptide; GDF-15 growth-differentiation-factor - 15; Gal-3 galectin-3. Variables with a p-value ≥ 0.05 for the association with the variable and outcome in multivariable analysis are not displayed. A higher X² score implies a stronger association with the outcome.