

Online supplementary Table 1. Multivariate Cox regression analyses for all-cause and cardiovascular mortality at 5 years including hs-cTnT

	All-cause death						Cardiovascular death					
	Gal-3			ST2			Gal-3			ST2		
	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
Age	1.04	[1.03 to 1.05]	<0.001	1.04	[1.02 to 1.05]	<0.001	1.03	[1.01 to 1.05]	<0.001	1.03	[1.01 to 1.05]	<0.001
Female	0.72	[0.55 to 0.94]	0.016	0.79	[0.60 to 1.04]	0.089	0.73	[0.5 to 1.07]	0.104	0.79	[0.54 to 1.15]	0.211
NYHA functional class	1.73	[1.36 to 2.2]	<0.001	1.66	[1.31 to 2.11]	<0.001	1.83	[1.33 to 2.53]	<0.001	1.86	[1.35 to 2.55]	<0.001
LVEF	1.01	[1 to 1.02]	0.156	1.01	[1 to 1.02]	0.148	1.01	[1 to 1.02]	0.127	1.01	[1 to 1.02]	0.109
Ischemic etiology of HF	1.13	[0.89 to 1.43]	0.324	1.14	[0.9 to 1.45]	0.265	1.37	[0.99 to 1.89]	0.058	1.34	[0.97 to 1.84]	0.079
Diabetes mellitus	1.07	[0.85 to 1.35]	0.550	1.07	[0.85 to 1.34]	0.573	1.15	[0.85 to 1.56]	0.375	1.12	[0.82 to 1.52]	0.469
eGFR, ml/min/1.73 m²	1	[0.99 to 1.01]	0.635	1	[0.99 to 1.01]	0.902	1	[0.99 to 1.01]	0.906	1	[0.99 to 1.01]	0.982
Na, mmol/L	0.97	[0.94 to 1]	0.096	0.98	[0.95 to 1.01]	0.213	0.94	[0.9 to 0.98]	0.003	0.93	[0.89 to 0.98]	0.002
Hb, g/dl	0.95	[0.89 to 1.02]	0.165	0.94	[0.88 to 1]	0.069	1.04	[0.95 to 1.15]	0.377	1.03	[0.94 to 1.13]	0.540
ACEI or ARB treatment	0.77	[0.56 to 1.06]	0.109	0.82	[0.8 to 1.15]	0.250	0.74	[0.49 to 1.13]	0.164	0.69	[0.45 to 1.06]	0.087
Beta-blocker treatment	0.54	[0.4 to 0.73]	<0.001	0.56	[0.41 to 0.75]	<0.001	0.52	[0.34 to 0.78]	0.001	0.52	[0.35 to 0.78]	0.001
Log (NT-proBNP)	1.19	[1.06 to 1.34]	0.004	1.14	[1.01 to 1.29]	0.029	1.17	[1 to 1.37]	0.051	1.16	[0.99 to 1.37]	0.075
Log(hs-cTnT)	5.07	[2.33 to 11.04]	<0.001	5.14	[2.37 to 11.2]	<0.001	9.36	[2.99 to 29.3]	<0.001	9.73	[3.12 to 30.3]	<0.001
Log (Gal-3)	1.27	[0.94 to 1.73]	0.119	-	-	-	1.22	[0.82 to 1.84]	0.327	-	-	-
ST2	-	-	-	1.24	[1.12 to 1.37]	<0.001	-	-	-	1.28	[1.06 to 1.55]	0.011

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blocker; eGFR = estimated glomerular filtration rate;

Gal-3 = Galectin 3; HF = heart failure; ST2 = high-sensitivity soluble ST2; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association (as III–IV functional class). The logarithmic functions of NT-proBNP and Gal-3 and the quadratic term of ST2 were used in the Cox models.

ST2 per every 10 ng/ml

P value for $(ST2^2) = 0.001$ for all-cause mortality and 0.019 for cardiovascular mortality. P value for $\text{Log}(\text{hs-cTnT})^2 < 0.001$ for all-cause mortality and < 0.001 for cardiovascular mortality in both models.

Online supplementary table 2. Performance of the models for all-cause mortality at 5 years including hs-cTnT in the reference model

	Reference model	Model with Gal-3	Model with ST2
<i>Discrimination</i>			
C-statistic	0.770	0.772	0.780
	(0.746 to 0.794)	(0.748 to 0.796)	(0.757 to 0.803)
	Reference	p = 0.208	p = 0.01
<i>Calibration</i>			
H-L	Chi-square: 15.9	Chi-square: 7.9	Chi-square: 6.7
	p = 0.07	p = 0.54	p = 0.67
Brier score	0.164	0.163	0.157
AIC	3884	3884	3869
BIC	3951	3955	3945
Likelihood ratio	Reference	p = 0.119	p < 0.001
<i>Reclassification</i>			
IDI		0.1 (-0.2 to 0.4)	1.5 (0.6 to 2.4)
	Reference	p = 0.492	p = 0.001
NRI - all		0.3 (-2.1 to 2.7)	4.4 (-0.1 to 8.8)
	Reference	p = 0.815	p = 0.054
NRI - deceased		1.4 (-0.5 to 3.3)	1.5 (-1.9 to 4.9)
	Reference	p = 0.159	p = 0.378
NRI - alive		-1.1 (-2.6 to 0.4)	2.8 (-0.1 to 5.8)
	Reference	p = 0.162	p = 0.062

All P values vs. reference model

Reference model: Age, Female, Ischemic etiology of heart failure, LVEF, NYHA functional class, Diabetes mellitus, eGFR, ACEI or ARB treatment, β -blocker treatment, sodium, hemoglobin, NT-proBNP and hs-cTnT

Model with Gal-3: Reference model + Gal-3

Model with ST2: Reference model + ST2

AIC = Akaike information criterion; BIC = Bayesian information criterion; Gal-3 = Galectin 3; H-L = Hosmer–Lemeshow test; hs-cTnT= high sensitivity circulating Troponin T; IDI = integrated discrimination improvement; NRI = net reclassification improvement; ST2 = high-sensitivity soluble ST2.

Online supplementary table 3. Performance of the models for cardiovascular mortality at 5 years including hs-cTnT in the reference model

	Reference model	Model with Gal-3	Model with ST2
<i>Discrimination</i>			
C-statistic	0.789 (0.760 to 0.817)	0.790 (0.762 to 0.819)	0.796 (0.768 to 0.823)
	Reference	p = 0.329	p = 0.059
<i>Calibration</i>			
H-L	Chi-square: 8.9 p = 0.49	Chi-square: 13.6 p = 0.14	Chi-square: 8.3 p = 0.50
Brier score	0.122	0.122	0.120
AIC	2177	2178	2170
BIC	2243	2249	2246
Likelihood ratio	Reference	p = 0.327	p = 0.005
<i>Reclassification</i>			
IDI	Reference	<0.1 (-0.3 to 0.4) p = 0.767	1.4 (0.5 to 2.3) p = 0.002
NRI - all	Reference	-0.1 (-2.5 to 2.2) p = 0.908	6.3 (1.7 to 10.9) p = 0.007
NRI - deceased	Reference	-1.1 (-3.1 to 1.0) p = 0.315	3.8 (-0.1 to 7.8) p = 0.058
NRI - alive	Reference	0.9 (-0.2 to 2.0) p = 0.101	2.5 (0.4 to 4.6) p = 0.02

All P values vs reference model

Reference model: Age, Female, Ischemic etiology of heart failure, LVEF, NYHA functional class, Diabetes mellitus, eGFR, ACEI or ARB treatment, β -blocker treatment, sodium, hemoglobin, NT-proBNP and hs-cTnT

Model with Gal-3: Reference Model + Gal-3

Model with ST2: Reference Model + ST2

AIC = Akaike information criterion; BIC = Bayesian information criterion; Gal-3 = Galectin 3; H-L = Hosmer–Lemeshow test; high sensitivity circulating Troponin T; IDI = integrated discrimination improvement; NRI = net reclassification improvement; ST2 = high-sensitivity soluble ST2.

Online supplementary table 4. Direct comparison of performance for all-cause and cardiovascular mortality at 5 years of models containing Gal-3 and ST2 including hs-cTnT in the models

	All-cause mortality		Cardiovascular mortality	
	Gal-3 vs. ST2		Gal-3 vs. ST2	
<i>Discrimination</i>				
C-statistic	0.772 (0.748 to 0.796)	0.780 (0.757 to 0.803)	0.790 (0.762 to 0.819)	0.796 (0.768 to 0.823)
	p = 0.040		p = 0.174	
<i>Calibration</i>				
H-L	Chi-square: 7.9 p = 0.54	Chi-square: 6.7 p = 0.67	Chi-square: 13.6 p = 0.14	Chi-square: 8.3 p = 0.50
Brier score	0.163	0.157	0.122	0.120
AIC	3884	3869	2178	2170
BIC	3955	3945	2249	2246
<i>Reclassification</i>				
IDI	Reference	1.4 (0.4 to 2.4) p = 0.006	Reference	1.3 (0.4 to 2.3) p = 0.005
NRI - all	Reference	5.0 (0.7 to 9.2) p = 0.022	Reference	6.8 (2.5 to 11.1) p = 0.002
NRI - deceased		0.2 (-3.1 to 3.4)		4.7 (1.1 to 8.3)

NRI - alive	Reference	p = 0.926	Reference	p = 0.011
		4.8 (2.0 to 7.7)		2.1 (<0.1 to 4.3)
	Reference	p < 0.001	Reference	p = 0.055

All P values vs reference model

All models include: Age, Female, Ischemic etiology of heart failure, LVEF, NYHA functional class, Diabetes mellitus, eGFR (estimated glomerular filtration rate), ACEI or ARB treatment, β -blocker treatment, sodium, hemoglobin, NT-proBNP and hs-cTnT.

Reference model = clinical factors + Gal-3; model with ST2=clinical factors + ST2.

AIC = Akaike information criterion; BIC= Bayesian information criterion; Gal-3 = Galectin 3; H-L = Hosmer–Lemeshow test; high sensitivity circulating Troponin T; IDI = integrated discrimination improvement; NRI = net reclassification improvement; ST2 = high-sensitivity soluble ST2.

Online Figure 1: Smoothing spline estimates for 5-year all-cause death for Gal-3 and ST2 non-transformed levels. Left: Galectin-3; Right: ST2

