

SUPPLEMENTAL MATERIAL

Supplemental Table 1. Baseline Characteristics in Patients with and without Complete Data

Characteristic	Complete (N=1631)	Incomplete (N=700)	p-value
Age	59.3 (51.3 - 68.2)	59.1 (50.9 - 67.6)	0.8261
Female, n (%)	464 (28)	197 (28)	0.8806
Race, n (%)			0.0002
Black	574 (35)	175/665 (26)	
White	978 (60)	448/665 (67)	
Other	79 (5)	42/665 (6)	
NYHA class at randomization, n (%)			0.8693
II	1036 (64)	441 (63)	
III	580 (36)	251 (36)	
IV	15 (1)	8 (1)	
Systolic blood pressure (mmHg)	N=1631	N=696	0.2315
Median (25 th , 75 th percentile)	112 (101 - 126)	110 (100 - 125)	
Diastolic blood pressure (mmHg)	N=1631	N=695	0.8398
Median (25 th , 75 th percentile)	70 (62 - 79)	70 (60 - 78)	
Rest heart rate (bpm)	N=1631	N=695	0.1876
Median (25 th , 75 th percentile)	70 (63 - 77)	70 (64 - 78)	
Ischemic etiology of HF, n (%)	824 (51)	373 (53)	0.2209
LVEF	N=1631	N=696	0.6093
Median (25 th , 75 th percentile)	25 (20 - 30)	25 (20 - 30)	
Mitral regurgitation, n (%)	203 (12)	53/504 (11)	0.2436
History of diabetes, n (%)	536 (33)	212 (30)	0.2217
Current smoking, n (%)	265 (16)	123/689 (18)	0.3441
History of hypertension, n (%)	1009 (62)	379/697 (54)	0.0004
History of MI, n (%)	671 (41)	308 (44)	0.1998
Hyperlipidemia, n (%)	1065 (65)	463/697 (66)	0.5990
History of a-fib or a-flutter, n (%)	351 (22)	137/699 (20)	0.2963
History of stroke, n (%)	170 (10)	68 (10)	0.6044
History of depression, n (%)	338 (21)	152 (22)	0.5905
Current CCS angina class, n (%)			0.2776
0	1354 (83)	596/697 (86)	
1	144 (9)	56/697 (8)	

≥ 2	133 (8)	45/697 (6)	
Highest level of education, n (%)			0.5253
Less than high school	185 (11)	100/648 (15)	
High school or equivalent	473 (29)	162/648 (25)	
Some college but no degree	434 (27)	175/648 (27)	
Associates degree or diploma	147 (9)	54/648 (8)	
College graduate	257 (16)	99/648 (15)	
Completed graduate school	135 (8)	58/648 (9)	
Married, n (%)	936 (57)	405/692 (59)	0.6116
Baseline medication and devices, n (%)			
Beta blocker	1545 (95)	658 (94)	0.4799
ACE-I/ARB	1538 (94)	661 (94)	0.9005
Loop diuretic	1299 (80)	517 (74)	0.0020
Aldosterone antagonist	738 (45)	313 (45)	0.8123
ICD	675 (41)	263 (38)	0.0852
Bi-ventricular pacemaker	300 (18)	119 (17)	0.4218
Functional measures			
Six-minute walk distance (meters)	N=1631	N=649	0.1665
Median (25 th , 75 th percentile)	368 (297 – 433)	375.8 (300 - 442)	
Exercise duration, CPX test (min)	N=1631	N=678	0.7514
Median (25 th , 75 th percentile)	9.7 (7 - 12)	9.5 (6.9 - 12)	
Peak VO ₂ in mL/kg/min, CPX test	N=1631	N=644	0.0172
Median (25 th , 75 th percentile)	14.3 (11.3 - 17.6)	14.8 (12 - 18.1)	
Laboratory values			
Sodium in mmol/L	N=1631	N=439	0.5821
Median (25 th , 75 th percentile)	139 (137 - 141)	139 (137 - 141)	
Creatinine in mg/dL	N=1631	N=460	0.9310
Median (25 th , 75 th percentile)	1.2 (1 - 1.5)	1.2 (1 - 1.42)	
Blood urea nitrogen in mg/dL	N=1631	N=394	0.4074
Median (25 th , 75 th percentile)	20 (15 - 28)	21 (16 - 29)	

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitor; a-fib, atrial fibrillation; ARB, angiotensin receptor blocker; a-flutter, atrial flutter; CCS, Canadian Cardiomyopathy Society; CPX, cardiopulmonary stress testing; HF, heart failure; ICD, internal cardioverter defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; VO₂, oxygen consumption

Supplemental Table 2. Model Comparisons for Death or Hospitalization Endpoint (Censored at 30 Months)

Predictors	Harrell C-index (95% CI)	NRI (95% CI) ^a	NRI for events (95% CI) ^a	NRI for non-events (95% CI) ^a	Additional cost, dollars	LR p-value
Model comparisons without NT proBNP (N=1631, 1031 events)						
Clinical information (C)	0.62 (0.60, 0.64)					
C + KCCQ total symptom score (K)	0.63 (0.61, 0.64)	0.017 (-0.036, 0.071)	-0.001 (-0.027, 0.025)	0.018 (-0.023, 0.059)	0.00	<0.0001
C + K + Laboratory assessments (L)	0.64 (0.62, 0.65)	0.045 (-0.009, 0.099)	0.002 (-0.027, 0.031)	0.043 (-0.006, 0.093)	11.63	<0.0001
C + K + L + Echocardiography parameters (E)	0.64 (0.63, 0.66)	0.055 (-0.007, 0.118)	0.007 (-0.028, 0.042)	0.048 (-0.003, 0.099)	201.14	<0.0001
C + K + L + E + Six-minute walk distance (S)	0.65 (0.63, 0.66)	0.079 (0.017, 0.141)	0.011 (-0.024, 0.046)	0.068 (0.023, 0.114)	258.30	<0.0001
C + K + L + E + S + Exercise parameters (full)	0.65 (0.64, 0.67)	0.109 (0.037, 0.181)	0.029 (-0.013, 0.071)	0.080 (0.026, 0.134)	425.69	<0.0001
Model comparisons with NT proBNP (N=1023, 646 events)						
Clinical information (C)	0.63 (0.61, 0.65)					
C + KCCQ total symptom score (K)	0.64 (0.61, 0.66)	0.016 (-0.036, 0.068)	0.000 (-0.026, 0.026)	0.016 (-0.025, 0.056)	0.00	0.0020
C + K + Laboratory assessments (L)	0.67 (0.64, 0.69)	0.113 (0.051, 0.174)	0.046 (0.002, 0.091)	0.066 (0.018, 0.114)	58.29	<0.0001
C + K + L + Echocardiography parameters (E)	0.67 (0.65, 0.69)	0.127 (0.057, 0.197)	0.045 (0.000, 0.090)	0.082 (0.029, 0.135)	247.80	<0.0001
C + K + L + E + Six-minute walk distance (S)	0.67 (0.65, 0.69)	0.140 (0.078, 0.202)	0.042 (-0.003, 0.086)	0.098 (0.055, 0.141)	304.96	<0.0001
C + K + L + E + S + Exercise parameters (full)	0.67 (0.65, 0.69)	0.162 (0.090, 0.233)	0.056 (0.007, 0.104)	0.106 (0.052, 0.160)	472.35	<0.0001

^aThe NRI compares each model to the model with clinical information only (C); it has 2 categories split at the incidence of death at 30 months, 0.14 in all patients and 0.13 in patients with non-missing NT-proBNP. The standard error for determining the 95% CI comes from the standard deviation of NRIs coming from 50 bootstrap samples with replacement.

Abbreviations: CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LR, likelihood ratio; NRI, Net Reclassification Index; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Supplemental Table 3. Model Comparisons for All-Cause Mortality Endpoint (Censored at 30 Months)

Predictors	Harrell C-index (95% CI)	NRI (95% CI) ^a	NRI for events (95% CI) ^a	NRI for non-events (95% CI) ^a	Additional cost, dollars	LR p-value
Model comparisons without NT-proBNP (n=1631, 223 events)						
Clinical information (C)	0.72 (0.68, 0.75)					
C + KCCQ total symptom score (K)	0.72 (0.68, 0.75)	0.001 (-0.030, 0.033)	0.000 (-0.028, 0.028)	0.001 (-0.012, 0.015)	0.00	0.1374
C + K + Laboratory assessments (L)	0.74 (0.70, 0.77)	0.039 (-0.034, 0.112)	0.000 (-0.060, 0.060)	0.039 (-0.005, 0.083)	11.63	<0.0001
C + K + L + Echocardiography parameters (E)	0.74 (0.71, 0.78)	0.045 (-0.043, 0.133)	0.000 (-0.064, 0.064)	0.045 (-0.002, 0.092)	201.14	<0.0001
C + K + L + E + Six-minute walk distance (S)	0.75 (0.72, 0.78)	0.061 (-0.024, 0.147)	0.004 (-0.066, 0.075)	0.057 (0.020, 0.094)	258.30	<0.0001
C + K + L + E + S + Exercise parameters (full)	0.77 (0.74, 0.80)	0.079 (0.001, 0.157)	0.009 (-0.060, 0.078)	0.070 (0.028, 0.112)	425.69	<0.0001
Model comparisons with NT-proBNP (n=1023, 134 events)						
Clinical information (C)	0.73 (0.69, 0.78)					
C + KCCQ total symptom score (K)	0.73 (0.69, 0.78)	-0.004 (-0.035, 0.026)	0.000 (-0.030, 0.030)	-0.004 (-0.020, 0.011)	0.00	0.7483
C + K + Laboratory assessments (L)	0.80 (0.76, 0.84)	0.091 (0.013, 0.169)	0.022 (-0.050, 0.094)	0.069 (0.025, 0.112)	58.29	<0.0001
C + K + L + Echocardiography parameters (E)	0.80 (0.77, 0.84)	0.082 (-0.011, 0.175)	0.022 (-0.056, 0.101)	0.060 (0.013, 0.106)	247.80	<0.0001
C + K + L + E + Six-minute walk distance (S)	0.81 (0.77, 0.84)	0.101 (0.014, 0.188)	0.030 (-0.050, 0.109)	0.071 (0.029, 0.113)	304.96	<0.0001
C + K + L + E + S + Exercise parameters (full)	0.81 (0.78, 0.85)	0.094 (0.005, 0.184)	0.022 (-0.060, 0.104)	0.072 (0.029, 0.115)	472.35	<0.0001

^aThe NRI compares each model to the model with clinical information only (C); it has 2 categories split at the incidence of death at 30 months, 0.14 in all patients and 0.13 in patients with non-missing NT-proBNP. The standard error for determining the 95% CI comes from the standard deviation of NRIs coming from 50 bootstrap samples with replacement.

Abbreviations: CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LR, likelihood ratio; NRI, Net Reclassification Index; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Supplemental Table 4. Model Comparisons for CV Death or HF Hospitalization Endpoint (Censored at 30 Months)

Predictors	Harrell C-index (95% CI)	NRI (95% CI) ^a	NRI for events (95% CI) ^a	NRI for non-events (95% CI) ^a	Additional cost, dollars	LR p-value
Model comparisons without NT proBNP (N=1631, 470 events)						
Clinical information (C)	0.68 (0.66, 0.71)					
C + KCCQ Total Symptom Score (K)	0.69 (0.66, 0.71)	0.009 (-0.035, 0.053)	-0.002 (-0.034, 0.029)	0.011 (-0.019, 0.041)	0.00	<0.0001
C + K + Laboratory assessments (L)	0.71 (0.68, 0.73)	0.045 (-0.022, 0.112)	0.015 (-0.029, 0.059)	0.030 (-0.008, 0.069)	11.63	<0.0001
C + K + L + Echocardiography parameters (E)	0.73 (0.70, 0.75)	0.076 (0.009, 0.144)	0.017 (-0.031, 0.065)	0.059 (0.012, 0.107)	201.14	<0.0001
C + K + L + E + Six-minute walk distance (S)	0.73 (0.71, 0.76)	0.094 (0.024, 0.165)	0.021 (-0.026, 0.069)	0.073 (0.027, 0.119)	258.30	<0.0001
C + K + L + E + S + Exercise parameters (full)	0.74 (0.72, 0.76)	0.115 (0.051, 0.180)	0.049 (0.000, 0.098)	0.066 (0.025, 0.108)	425.69	<0.0001
Model comparisons with NT proBNP (N=1023, 304 events)						
Clinical information (C)	0.68 (0.65, 0.71)					
C + KCCQ Total Symptom Score (K)	0.69 (0.66, 0.72)	0.008 (-0.039, 0.055)	-0.013 (-0.051, 0.025)	0.021 (-0.007, 0.049)	0.00	0.0005
C + K + Laboratory assessments (L)	0.75 (0.73, 0.78)	0.133 (0.069, 0.197)	0.049 (-0.002, 0.100)	0.083 (0.044, 0.123)	58.29	<0.0001
C + K + L + Echocardiography parameters (E)	0.76 (0.73, 0.79)	0.139 (0.081, 0.197)	0.053 (0.006, 0.099)	0.086 (0.043, 0.130)	247.80	<0.0001
C + K + L + E + Six-minute walk distance (S)	0.76 (0.73, 0.79)	0.151 (0.094, 0.208)	0.053 (0.009, 0.097)	0.099 (0.057, 0.141)	304.96	<0.0001
C + K + L + E + S + Exercise parameters (full)	0.76 (0.74, 0.79)	0.164 (0.107, 0.221)	0.063 (0.015, 0.110)	0.102 (0.058, 0.145)	472.35	<0.0001

^aThe NRI compares each model to the model with clinical information only (C); it has 2 categories split at the incidence of CV death or HF hospitalization at 30 months, 0.29 all patients and 0.30 in patients with non-missing NT-proBNP. The standard error for determining the 95% CI comes from the standard deviation of NRIs coming from 50 bootstrap samples with replacement.

Abbreviations: CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LR, likelihood ratio; NRI, Net Reclassification Index; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Supplemental Table 5. Current Prediction Models and Variables Used

Variable/Label	DF	Wald Chi-Square	Probability Chi-Square
Five most significant of added variables in <u>death or rehospitalization</u> endpoint (without NT-proBNP)			
KCCQ total symptom score at baseline	1	9.6121	0.0019
Mitral regurgitation grade	1	9.5303	0.0020
Peak VO ₂	1	8.8083	0.0030
Creatinine	1	7.0696	0.0078
Exercise duration, CPX test (minutes)	1	5.5472	0.0185
Five most significant of added variables in <u>death or rehospitalization</u> endpoint (with NT-proBNP)			
Log (NT-proBNP)	1	17.7853	<0.0001
KCCQ total symptom score at baseline	1	5.6253	0.0177
Exercise duration, CPX test (minutes)	1	4.4923	0.0340
Creatinine	1	3.4793	0.0621
LVEF	1	1.9280	0.1650
Five most significant of added variables in <u>death</u> endpoint (without NT-proBNP)			
Mitral regurgitation grade	1	8.6368	0.0033
Exercise duration, CPX test (minutes)	1	5.5665	0.0183
Creatinine	1	5.2462	0.0220
Peak VO ₂ in mL/kg/min, CPX test	1	2.2200	0.1362
6-minute walk distance (meters), subjects able to walk	1	1.5093	0.2192
Five most significant of added variables in <u>death</u> endpoint (with NT-proBNP)			
Log (NT-proBNP)	1	21.6152	<0.0001
Blood urea nitrogen in mg/dL	1	3.7800	0.0519
Exercise duration, CPX test (minutes)	1	2.6402	0.1042
Mitral regurgitation grade	1	2.2410	0.1344
6-minute walk distance (meters), subjects able to walk	1	1.6877	0.1939
Five most significant of added variables in <u>CV death/CV hospitalization</u> endpoint (without NT-proBNP)			
Mitral regurgitation grade	1	17.2779	<0.0001
LVEF	1	16.5280	<0.0001
KCCQ total symptom score at baseline	1	11.0565	0.0009
Exercise duration, CPX test (minutes)	1	3.8128	0.0509
6-minute walk distance, linear spline below 450	1	2.8073	0.0938

Five most significant of added variables in CV death/CV hospitalization endpoint
(including NT-proBNP)

Log (NT-proBNP)	1	27.7975	<0.0001
KCCQ total symptom score at baseline	1	9.6313	0.0019
LVEF	1	5.3356	0.0209
Mitral regurgitation grade	1	4.7922	0.0286
Exercise duration, CPX test (minutes)	1	2.8436	0.0917

Five most significant of added variables in CV death/HF hospitalization endpoint
(without NT-proBNP)

Mitral regurgitation grade	1	28.6995	<0.0001
LVEF	1	12.2900	0.0005
KCCQ total symptom score at baseline	1	8.1082	0.0044
Peak VO ₂ in mL/kg/min, CPX test	1	6.8651	0.0088
6-minute walk distance (meters), subjects able to walk	1	3.7015	0.0544

Five most significant of added variables in CV death/HF hospitalization endpoint
(including NT-proBNP)

Log (NT-proBNP)	1	28.8347	<0.0001
Mitral regurgitation grade	1	11.3893	0.0007
KCCQ total symptom score at baseline	1	6.1648	0.0130
BUN	2	3.7597	0.1526
6-minute walk distance (meters), subjects able to walk	1	1.8773	0.1706

Abbreviations: BUN, blood urea nitrogen; CPX, cardiopulmonary stress testing; CV, cardiovascular; DF, degree of freedom; HF, heart failure; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; VO₂, oxygen consumption

Supplemental Table 6. Model Comparisons for All-Cause Death and Hospitalization Endpoint (Censored at 30 Months)

Predictors	Harrell C-index (95% CI)	NRI (95% CI) ^a	NRI for events (95% CI) ^a	NRI for non- events (95% CI) ^a	Additional cost, dollars	LR p-value
Model comparisons without NT proBNP (N=1631, 1031 events)						
Clinical information (C)	0.62 (0.60, 0.64)					
C + KCCQ Total Symptom Score (K)	0.63 (0.61, 0.64)	0.017 (-0.036, 0.071)	-0.001 (-0.027, 0.025)	0.018 (-0.023, 0.059)	0.00	<0.0001
C + K + Six-minute walk distance (S)	0.63 (0.62, 0.65)	0.017 (-0.039, 0.072)	-0.012 (-0.036, 0.013)	0.028 (-0.019, 0.075)	258.30	<0.0001
C + K + S + Laboratory assessments (L)	0.64 (0.62, 0.66)	0.065 (0.004, 0.126)	0.000 (-0.032, 0.032)	0.065 (0.015, 0.115)	11.63	<0.0001
C + K + S + L + Echocardiography parameters (E)	0.65 (0.63, 0.66)	0.079 (0.017, 0.141)	0.011 (-0.024, 0.046)	0.068 (0.023, 0.114)	201.14	<0.0001
C + K + S + L + E + Exercise parameters (full)	0.65 (0.64, 0.67)	0.109 (0.037, 0.181)	0.029 (-0.013, 0.071)	0.080 (0.026, 0.134)	425.69	<0.0001
Model comparisons with NT proBNP (N=1023, 646 events)						
Clinical information (C)	0.63 (0.61, 0.65)					
C + KCCQ Total Symptom Score (K)	0.64 (0.61, 0.66)	0.016 (-0.036, 0.068)	0.000 (-0.026, 0.026)	0.016 (-0.025, 0.056)	0.00	0.0020
C + K + Six-minute walk distance (S)	0.64 (0.62, 0.67)	0.016 (-0.040, 0.071)	0.008 (-0.016, 0.031)	0.008 (-0.040, 0.056)	304.96	<0.0001
C + K + S + Laboratory assessments (L)	0.67 (0.65, 0.69)	0.130 (0.067, 0.194)	0.040 (-0.002, 0.083)	0.090 (0.041, 0.139)	58.29	<0.0001

C + K + S + L + Echocardiography parameters (E)	0.67 (0.65, 0.69)	0.140 (0.078, 0.202)	0.042 (-0.003, 0.086)	0.098 (0.055, 0.141)	247.80	<0.0001
C + K + S + L + E + Exercise parameters (full)	0.67 (0.65, 0.69)	0.162 (0.090, 0.233)	0.056 (0.007, 0.104)	0.106 (0.052, 0.160)	472.35	<0.0001

^aThe NRI compares each model to the model with clinical information only (C); it has 2 categories split at the incidence of death at 30 months, 0.14 in all patients and 0.13 in patients with non-missing NT-proBNP. The standard error for determining the 95% CI comes from the standard deviation of NRIs coming from 50 bootstrap samples with replacement.

Abbreviations: CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LR, likelihood ratio; NRI, Net Reclassification Index; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Supplemental Table 7. Model Comparisons for All-Cause Death Endpoint (Censored at 30 Months)

Predictors	Harrell C-index (95% CI)	NRI (95% CI) ^a	NRI for events (95% CI) ^a	NRI for non- events (95% CI) ^a	Additional cost, dollars	LR p-value
Model comparisons without NT proBNP (N=1631, 223 events)						
Clinical information (C)	0.72 (0.68, 0.75)					
C + KCCQ Total Symptom Score (K)	0.72 (0.68, 0.75)	0.001 (-0.030, 0.033)	0.000 (-0.028, 0.028)	0.001 (-0.012, 0.015)	0.00	0.1374
C + K + Six-minute walk distance (S)	0.73 (0.70, 0.76)	0.007 (-0.062, 0.076)	-0.018 (-0.076, 0.040)	0.025 (0.000, 0.050)	258.30	<0.0001
C + K + S + Laboratory assessments (L)	0.74 (0.71, 0.78)	0.056 (-0.016, 0.128)	0.009 (-0.057, 0.075)	0.047 (0.010, 0.083)	11.63	<0.0001
C + K + S + L + Echocardiography parameters (E)	0.75 (0.72, 0.78)	0.061 (-0.024, 0.147)	0.004 (-0.066, 0.075)	0.057 (0.020, 0.094)	201.14	<0.0001
C + K + S + L + E + Exercise parameters (full)	0.77 (0.74, 0.80)	0.079 (0.001, 0.157)	0.009 (-0.060, 0.078)	0.070 (0.028, 0.112)	425.69	<0.0001
Model comparisons with NT proBNP (N=1023, 134 events)						
Clinical information (C)	0.73 (0.69, 0.78)					
C + KCCQ Total Symptom Score (K)	0.73 (0.69, 0.78)	-0.004 (-0.035, 0.026)	0.000 (-0.030, 0.030)	-0.004 (-0.020, 0.011)	0.00	0.7483
C + K + Six-minute walk distance (S)	0.75 (0.71, 0.79)	0.014 (-0.051, 0.079)	-0.007 (-0.065, 0.050)	0.021 (-0.004, 0.046)	304.96	0.0010

C + K + S + Laboratory assessments (L)	0.81 (0.77, 0.84)	0.085 (0.006, 0.164)	0.015 (-0.058, 0.088)	0.070 (0.031, 0.108)	58.29	<0.0001
C + K + S + L + Echocardiography parameters (E)	0.81 (0.77, 0.84)	0.101 (0.014, 0.188)	0.030 (-0.050, 0.109)	0.071 (0.029, 0.113)	247.80	<0.0001
C + K + S + L + E + Exercise parameters (full)	0.81 (0.78, 0.85)	0.094 (0.005, 0.184)	0.022 (-0.060, 0.104)	0.072 (0.029, 0.115)	472.35	<0.0001

^aThe NRI compares each model to the model with clinical information only (C); it has 2 categories split at the incidence of death at 30 months, 0.14 in all patients and 0.13 in patients with non-missing NT-proBNP. The standard error for determining the 95% CI comes from the standard deviation of NRIs coming from 50 bootstrap samples with replacement.

Abbreviations: CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LR, likelihood ratio; NRI, Net Reclassification Index; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Supplemental Table 8. Model comparisons for CV death or HF hospitalization endpoint (censored at 30 months)

Predictors	Harrell C-index (95% CI)	NRI (95% CI) ^a	NRI for events (95% CI) ^a	NRI for non-events (95% CI) ^a	Additional cost, dollars	LR p-value
Model comparisons without NT proBNP (N=1631, 470 events)						
Clinical information (C)	0.68 (0.66, 0.71)					
C + KCCQ Total Symptom Score (K)	0.69 (0.66, 0.71)	0.009 (-0.035, 0.053)	-0.002 (-0.034, 0.029)	0.011 (-0.019, 0.041)	0.00	<0.0001
C + K + Six-minute walk distance (S)	0.70 (0.67, 0.72)	0.026 (-0.024, 0.076)	0.000 (-0.036, 0.036)	0.026 (-0.011, 0.063)	258.30	<0.0001
C + K + S + Laboratory assessments (L)	0.71 (0.69, 0.74)	0.056 (-0.009, 0.121)	0.000 (-0.045, 0.045)	0.056 (0.018, 0.094)	11.63	<0.0001
C + K + S + L + Echocardiography parameters (E)	0.73 (0.71, 0.76)	0.094 (0.024, 0.165)	0.021 (-0.026, 0.069)	0.073 (0.027, 0.119)	201.14	<0.0001
C + K + S + L + E + Exercise parameters (full)	0.74 (0.72, 0.76)	0.115 (0.051, 0.180)	0.049 (0.000, 0.098)	0.066 (0.025, 0.108)	425.69	<0.0001
Model comparisons with NT proBNP (N=1023, 304 events)						
Clinical information (C)	0.68 (0.65, 0.71)					
C + KCCQ Total Symptom Score (K)	0.69 (0.66, 0.72)	0.008 (-0.039, 0.055)	-0.013 (-0.051, 0.025)	0.021 (-0.007, 0.049)	0.00	0.0005
C + K + Six-minute walk distance (S)	0.70 (0.67, 0.73)	0.056 (0.003, 0.108)	0.020 (-0.017, 0.056)	0.036 (0.005, 0.068)	304.96	<0.0001

C + K + S + Laboratory assessments (L)	0.75 (0.73, 0.78)	0.153 (0.097, 0.210)	0.056 (0.008, 0.104)	0.097 (0.060, 0.135)	58.29	<0.0001
C + K + S + L + Echocardiography parameters (E)	0.76 (0.73, 0.79)	0.151 (0.094, 0.208)	0.053 (0.009, 0.097)	0.099 (0.057, 0.141)	247.80	<0.0001
C + K + S + L + E + Exercise parameters (full)	0.76 (0.74, 0.79)	0.164 (0.107, 0.221)	0.063 (0.015, 0.110)	0.102 (0.058, 0.145)	472.35	<0.0001

^aThe NRI compares each model to the model with clinical information only (C); it has 2 categories split at the incidence of death at 30 months, 0.14 in all patients and 0.13 in patients with non-missing NT-proBNP. The standard error for determining the 95% CI comes from the standard deviation of NRIs coming from 50 bootstrap samples with replacement.

Abbreviations: CI, confidence interval; KCCQ, Kansas City Cardiomyopathy Questionnaire; LR, likelihood ratio; NRI, Net Reclassification Index; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Supplemental Table 9. Current Prediction Models and Variables Used

Risk Score	Variables Used	Outcome	C-Statistic
CHARM ¹	<ul style="list-style-type: none"> • Age • Ejection fraction • DM • BMI • Female sex • NYHA class III/IV • Current smoker • Bundle branch block • Cardiomegaly • Prior HF hospitalization • DBP • Diagnosis of HF • Previous MI • Dependent edema • HR • Pulmonary crackles • Pulmonary edema • Mitral regurgitation • AF • Rest dyspnea • Candesartan 	All-cause mortality	0.75
CORONA ²	<ul style="list-style-type: none"> • NT-proBNP • Age • DM • LVEF • BMI • CABG • Female sex • AF • NYHA class • ApoA-1 • Serum creatinine • Intermittent claudication • HR • MI 	All-cause mortality	0.72
HF Survival Score ³	<ul style="list-style-type: none"> • Ischemic cardiomyopathy • Resting HR LVEF • IVCD (QRS duration ≥ 0.12 second of any cause) • Mean resting blood pressure • Peak $\dot{V}O_2$ • Serum sodium 	All-cause mortality	0.56–0.79

Seattle HF Model ⁴	<ul style="list-style-type: none"> • Age • Sex • Ischemic etiology • NYHA class • Ejection fraction • SBP • Potassium-sparing diuretic use • Statin use • Allopurinol use • Hemoglobin • % lymphocyte count • Uric acid • Sodium • Cholesterol • Diuretic dose/kg 	All-cause mortality	0.73
HF-ACTION Predictive Risk Score Model (abbreviated) ⁵	<ul style="list-style-type: none"> • Exercise duration • BUN • Sex • BMI 	All-cause mortality	0.73
HF-ACTION Predictive Risk Score Model (full) ⁵	<ul style="list-style-type: none"> • Sex • Race • BUN • BMI • DBP • KCCQ • LVEF • Exercise duration • Ventricular conduction • Mitral regurgitation 	All-cause mortality	0.74
Incremental value score Baseline clinical assessment and QOL	<ul style="list-style-type: none"> • Age • Sex • Race • SBP • DBP • HR • BMI • NYHA class • DM • Dyslipidemia • COPD • PVD • AF • Stroke • Depression • Prior HF hospitalization 	All-cause mortality	0.73

	<ul style="list-style-type: none"> • HF etiology • CCS angina class • Education level • Marital and employment status • KCCQ 	
+ Laboratory assessments including NT-proBNP)	<ul style="list-style-type: none"> • Sodium • Creatinine • BUN • NT-proBNP 	0.80
+ Echocardiographic parameters	<ul style="list-style-type: none"> • LVEF • Mitral regurgitation 	0.80
+ Exercise parameters	<ul style="list-style-type: none"> • Peak VO₂ • Exercise duration • 6MWD 	0.81

Abbreviations: AF, atrial fibrillation; ApoA-1, apolipoprotein A-1; BMI, body mass index; BUN, blood urea nitrogen; CABG, coronary artery bypass grafting; CCS, Canadian Cardiomyopathy Society; CHARM, Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity; COPD, chronic obstructive pulmonary disease; CORONA, Controlled Rosuvastatin Multinational Study in Heart Failure; DBP, diastolic blood pressure; DM, diabetes mellitus; HF, heart failure; HR, heart rate; IVCD, intraventricular conduction delay; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; PVD, peripheral vascular disease; SBP, systolic blood pressure; VO₂, oxygen consumption; 6MWD, six-minute walk distance

Supplemental References

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