

Supplemental Material

Supplemental Table 1. Potential Covariates in HF-ACTION Predictive Models for Primary Endpoint

| | Variable |
|----|---|
| 1 | Age |
| 2 | Sex |
| 3 | Race |
| 4 | History of myocardial infarction |
| 5 | Previous revascularization |
| 6 | History of diabetes |
| 7 | History of peripheral vascular disease |
| 8 | Smoking status |
| 9 | History of chronic obstructive pulmonary disease |
| 10 | Heart failure hospitalizations in last 6 months |
| 11 | Hospitalizations in last 6 months |
| 12 | Etiology of heart failure |
| 13 | New York Heart Association Class (II versus III/IV) |
| 14 | Canadian Angina Class |
| 15 | Baseline automated implantable cardioverter/defibrillator |
| 16 | Baseline biventricular pacemaker |
| 17 | Baseline pacemaker |
| 18 | Atrial fibrillation/flutter |
| 19 | Mitral regurgitation grade by echocardiography |
| 20 | Systolic blood pressure |
| 21 | Diastolic blood pressure |
| 22 | Baseline heart rate |
| 23 | Body mass index |
| 24 | Left ventricular ejection fraction |
| 25 | KCCQ: total symptom score |
| 26 | KCCQ: quality of life score |
| 27 | KCCQ: self-efficacy score |
| 28 | KCCQ: symptom stability score |
| 29 | KCCQ: physical limitation score |
| 30 | KCCQ: social limitation score |

Supplemental Table 1. Potential Covariates in HF-ACTION Predictive Models for Primary Endpoint

| | Variable |
|----|--|
| 31 | Beck Depression Index II |
| 32 | Heart rate reserve on CPX test |
| 33 | Heart rate at peak exercise on CPX test |
| 34 | Heart rate at end of 2 nd stage of CPX test |
| 35 | Exercise duration on CPX test |
| 36 | Rest ECG rhythm on CPX test |
| 37 | Peak oxygen pulse on CPX test |
| 38 | Peak respiratory exchange ratio on CPX test |
| 39 | Ventricular conduction prior to CPX test |
| 40 | V_E/V_{CO_2} slope |
| 41 | Peak VO_2 |
| 42 | Weber class |
| 43 | Six-minute walk distance |
| 44 | Serum creatinine |
| 45 | Sodium |
| 46 | Blood urea nitrogen |
| 47 | Hemoglobin |
| 48 | Treatment group (exercise vs. usual care) |

CPX, cardiopulmonary exercise test; ECG, electrocardiogram; KCCQ, Kansas City Cardiomyopathy Questionnaire; V_E/V_{CO_2} , volume of air exhaled/volume of CO_2 exhaled; VO_2 , oxygen consumption

Supplemental Table 2. Full Predictive Model for Primary Endpoint

| Parameter | Average χ^2 | <i>P</i> | HR (CI) |
|---|------------------|----------|------------------|
| Blood urea nitrogen (HR for 10 mg/dL increase) | 30.4 | <0.0001 | 1.07 (1.04-1.09) |
| KCCQ symptom stability | | | |
| Much worse/slightly worse | 34.1 | <0.0001 | 1.65 (1.38-1.97) |
| Much better/slightly better | | | 1.22 (1.07-1.39) |
| KCCQ total symptom score (HR for 5-unit increase) | 23.4 | <0.0001 | 0.97 (0.96-0.98) |
| Weber class | | | |
| B (Peak VO ₂ 16.1-20) | | | 0.96 (0.77-1.19) |
| C (Peak VO ₂ 10.1-16) | 26.0 | <0.0001 | 1.36 (1.09-1.69) |
| D (Peak VO ₂ ≤10) | | | 1.55 (1.17-2.05) |
| Left ventricular ejection fraction (HR for 5% increase) | 18.0 | <0.0001 | 0.93 (0.89-0.96) |
| Exercise duration on CPX test (HR for 1-min increase) | 17.3 | <0.0001 | 0.96 (0.94-0.98) |
| Ventricular conduction prior to CPX | | | |
| Left bundle branch block | | | 1.07 (0.92-1.25) |
| Right bundle branch block | 24.3 | 0.0001 | 1.38 (1.07-1.77) |
| Intraventricular conduction delay | | | 1.24 (1.06-1.46) |
| Paced | | | 1.35 (1.18-1.54) |
| Sex: female | 15.0 | 0.0001 | 0.79 (0.70-0.89) |
| Mitral regurgitation: severe | 13.7 | 0.0002 | 1.32 (1.14-1.52) |
| Race | | | |
| Black or African American | 5.7 | 0.0575 | 1.11 (0.99-1.25) |
| Other | | | 1.24 (0.99-1.56) |

CI, confidence interval; CPX test, cardiopulmonary exercise test; HR, hazard ratio; KCCQ, Kansas City Cardiomyopathy Questionnaire; VO₂, oxygen consumption.

Reference categories: KCCQ symptom stability=no change or no symptoms; Weber Class=A; ventricular conduction=normal; sex=male; mitral regurgitation=non-severe/none; race= white

Supplemental Table 3. Full Predictive Model for Mortality Endpoint

| Parameter | Average χ^2 | P value | HR (CI) |
|---|------------------|---------|------------------|
| Exercise duration on CPX test (HR for 1-min increase) | 118.0 | <0.0001 | 0.84 (0.81-0.86) |
| Sex: female | 18.2 | <0.0001 | 0.56 (0.43-0.73) |
| BMI (HR for a 2 kg/m ² increase, truncated above 25) | 13.5 | 0.0002 | 0.80 (0.70-0.90) |
| Serum creatinine (HR for 0.1 mg/dL increase, truncated above 2.3) | 12.1 | 0.0005 | 1.04 (1.02-1.07) |
| Mitral regurgitation: severe | 7.9 | 0.0049 | 1.45 (1.12-1.88) |
| Left ventricular ejection fraction (HR for 5% increase) | 7.8 | 0.0051 | 0.90 (0.84-0.97) |
| Blood urea nitrogen (HR for 10 mg/dL increase) | 6.7 | 0.0097 | 1.06 (1.01-1.10) |
| Ventricular conduction prior to CPX | | | |
| Left bundle branch block | | | 0.76 (0.55-1.06) |
| Right bundle branch block | 12.9 | 0.0120 | 1.35 (0.86-2.12) |
| Intraventricular conduction delay | | | 1.09 (0.79-1.51) |
| Paced | | | 1.32 (1.02-1.71) |
| Diastolic blood pressure (HR for 5 mm Hg increase) | 5.6 | 0.0175 | 0.94 (0.90-0.99) |
| Canadian Angina Classification | | | |
| 1 | | | 1.23 (0.87-1.74) |
| ≥2 | 6.8 | 0.0338 | 0.62 (0.40-0.94) |

BMI, body mass index; CI, confidence interval; CPX test, cardiopulmonary exercise test; Hg, mercury; HR., hazard ratio;

Reference categories: Sex=male; mitral regurgitation=non-severe/none; ventricular conduction=normal; Canadian Angina Classification=0