

Supplemental Material

Supplemental Table 1. Characteristics of the BIOSTAT population by Coronary Stenosis Findings

	No Coronary Stenosis (n=190)	Coronary Stenosis (n=122)	P-value
Age, years	61.7 ± 12.0	66.7 ± 10.3	0.0002
Male gender, n (%)	128 (67.4 %)	97 (79.5 %)	0.020
BMI, kg/m ²	28.5 ± 6.5	27.8 ± 5.5	0.32
Heart rate, bpm	88.4 ± 20.3	86.0 ± 23.2	0.34
SBP, mmHg	123.3 ± 23.3	128.2 ± 24.4	0.080
DBP, mmHg	76.4 ± 15.6	76.0 ± 16.2	0.80
Pulmonary rales, n (%)	106 (56.7 %)	82 (68.9 %)	0.032
Peripheral edema, n (%)	90 (58.8 %)	58 (59.2 %)	0.95
Elevated JVP, n (%)	39 (31.7 %)	34 (36.6 %)	0.46
NYHA class III/IV, n (%)	119 (64.7 %)	77 (65.8 %)	0.84
Orthopnea, n (%)	85 (44.7 %)	49 (40.2 %)	0.43
LVEF, %	27.8 ± 9.2	29.9 ± 10.2	0.070
Northern Europe, n (%)	102 (53.7 %)	48 (39.3 %)	0.013
HHF within the last year, n (%)	28 (14.7 %)	15 (12.3 %)	0.54
HF etiology: Ischemic, n (%)	16 (8.4 %)	98 (80.3 %)	<0.0001
HF etiology: Hypertensive, n (%)	26 (13.7 %)	2 (1.6 %)	
HF etiology: Valvular, n (%)	14 (7.4 %)	7 (5.7 %)	
HF etiology: Other/mixed, n (%)	134 (70.5 %)	15 (12.3 %)	
Coronary angiography, n (%)	190 (100.0 %)	122 (100.0 %)	NA
Hemoglobin, g/dL	13.8 ± 1.8	13.2 ± 2.0	0.009
eGFR, ml/min/1.73m ²	71.2 ± 21.8	66.6 ± 21.3	0.064
Urea, mmol/L	8.9 (6.5 - 15.0)	9.2 (6.8 - 14.5)	0.67
Sodium, mmol/L	139.4 ± 3.8	138.9 ± 3.4	0.20
Potassium, mmol/L	4.1 ± 0.5	4.2 ± 0.6	0.42
Albumin, g/L	32.4 ± 8.3	32.1 ± 7.1	0.72
Glucose, mmol/L	7.0 ± 2.5	7.9 ± 3.2	0.013
ALAT, UI/L	33.0 (22.0 - 51.0)	30.0 (20.0 - 46.0)	0.10
ASAT, UI/L	29.0 (22.0 - 43.0)	27.0 (21.0 - 41.0)	0.58
Gamma-GT, UI/L	57.0 (28.0 - 118.0)	54.0 (29.0 - 88.0)	0.44
Total bilirubin, µmol/L	15.7 (10.3 - 20.8)	11.8 (10.0 - 19.0)	0.041
HDL, mmol/L	1.1 ± 0.3	1.2 ± 0.4	0.48
LDL, mmol/L	2.7 ± 1.0	2.9 ± 1.2	0.29
Total cholesterol, mmol/L	4.5 ± 1.2	4.5 ± 1.3	0.77
Triglycerides, mmol/L	1.5 ± 1.1	1.3 ± 0.7	0.19
LogNT-pro BNP, ng/L	2.8 ± 1.2	3.1 ± 1.1	0.045
Troponin I, pg/mL	13.2 (6.8 - 36.0)	36.0 (12.9 - 36.0)	<0.0001
Hypertension, n (%)	104 (54.7 %)	81 (66.4 %)	0.041
Atrial Fibrillation, n (%)	62 (32.6 %)	36 (29.5 %)	0.56
Diabetes mellitus, n (%)	54 (28.4 %)	47 (38.5 %)	0.063
Never smoked, n (%)	72 (37.9 %)	29 (24.0 %)	0.038
Past smoker, n (%)	76 (40.0 %)	59 (48.8 %)	
Current smoker, n (%)	42 (22.1 %)	33 (27.3 %)	
COPD, n (%)	27 (14.2 %)	22 (18.0 %)	0.37

Stroke, n (%)	8 (4.2 %)	8 (6.6 %)	0.36
Peripheral Artery Disease, n (%)	11 (5.8 %)	16 (13.1 %)	0.025
Device therapy, n (%)	13 (6.8 %)	14 (11.5 %)	0.16
PCI or CABG, n (%)	13 (6.8 %)	54 (44.3 %)	<0.0001
Loop diuretic, n (%)	187 (98.4 %)	121 (99.2 %)	0.95
ACEi/ARB, n (%)	144 (75.8 %)	100 (82.0 %)	0.20
Beta-blocker, n (%)	158 (83.2 %)	104 (85.2 %)	0.62
MRA, n (%)	100 (52.6 %)	58 (47.5 %)	0.38
Digoxin, n (%)	33 (17.4 %)	16 (13.1 %)	0.31
Death or HHF, n (%)	40 (21.1 %)	43 (35.2 %)	0.006
Death, n (%)	17 (8.9 %)	26 (21.3 %)	0.002
HHF, n (%)	26 (13.7 %)	23 (18.9 %)	0.22

Legend: MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure; JVP, jugular venous pressure; NYHA, New York Heart Association; H, hospitalization; HF, heart failure; eGFR, estimated glomerular filtration rate; NT-pro BNP, n-terminal pro brain natriuretic peptide; COPD, chronic pulmonary obstructive disease; PCI or CABG, percutaneous coronary intervention or coronary artery bypass grafting; ACEi/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker.

Supplemental Table 2. Prognostic capacity of Troponin I

Variable	TnI: unadjusted HR (95%CI) per 1 pg/mL increase	C-index	P-value	TnI: adjusted* HR (95%CI) per 1 pg/mL increase	C-index	P-value
Death or HHF	1.026 (1.021-1.031)	0.62	<0.0001	1.016 (1.010-1.021)	0.72	<0.0001
HHF	1.024 (1.017-1.031)	0.61	<0.0001	1.016 (1.009-1.023)	0.70	<0.0001
Death	1.033 (1.026-1.039)	0.64	<0.0001	1.020 (1.013-1.027)	0.75	<0.0001

Legend: TnI, troponin I; HR, hazard ratio; 95%CI, 95% confidence interval; HHF, heart failure hospitalization.

*model adjusted on age, race, gender, NT-pro BNP, hemoglobin, urea, HDL-cholesterol, serum sodium, serum creatinine, systolic blood pressure, use of beta-blockers, presence of peripheral edema, and hospitalization for heart failure in the year before inclusion – the BIOSTAT risk model.

No interaction was present between Troponin I levels AND reaching target dose of ACEi/ARBs (p=0.34) or Beta-blockers (p=0.52) at 3 months (selecting only patients who reached the 3-month visit).

Supplemental Table 3. C-index comparison between the BIOSTAT risk models and the BIOSTAT risk models plus Troponin I

Endpoint	C-index BIOSTAT risk model	LR	C-index BIOSTAT risk model + TnI	LR
Death or HHF	0.71	274	0.73	379
HHF	0.69	223	0.70	243
Death	0.74	397	0.75	429

Legend: HHF, heart failure hospitalization; TnI, troponin I; LR, likelihood ratio test.

BIOSTAT risk models for each outcome at 2 years of follow-up include age, race, gender, NT-pro BNP, hemoglobin, urea, HDL-cholesterol, serum sodium, serum creatinine, systolic blood pressure, use of beta-blockers, presence of peripheral edema, and hospitalization for heart failure in the year before inclusion (available at: <https://biostat-chf.shinyapps.io/calc/>)

Supplemental Table 4. Coronary angiography performance by country

	No Coronary Angiography (n=2201)	Coronary Angiography (n=315)	Total
Netherlands	326	81	407
% within Country	80.1%	19.9%	100%
% within Total	14.8%	25.7%	16.2%
France	214	49	263
% within Country	81.4%	18.6%	100%
% within Total	9.7%	15.6%	10.5%
Germany	71	19	90
% within Country	78.9%	21.1%	100%
% within Total	3.2%	6%	3.6%
Serbia	361	24	385
% within Country	93.8%	6.2%	100%
% within Total	16.4%	7.6%	15.3%
Slovenia	43	2	45
% within Country	95.6%	4.4%	100%
% within Total	2.00%	0.6%	1.8%
Greece	271	33	304
% within Country	89.1%	10.9%	100%
% within Total	12.3%	10.5%	12.1%
Italy	277	42	319
% within Country	86.8%	13.2%	100%
% within Total	12.6%	13.3%	12.7%
Norway	98	11	109
% within Country	89.9%	10.1%	100%
% within Total	4.5%	3.5%	4.3%
Sweden	96	6	102
% within Country	94.1%	5.9%	100%
% within Total	4.4%	1.9%	4.1%
Poland	271	25	296
% within Country	91.6%	8.4%	100%
% within Total	12.3%	7.9%	11.8%
UK	173	23	196
% within Country	88.3%	11.7%	100%
% within Total	7.9%	7.3%	7.8%

Supplemental Figure 1. Coronary angiography. Odds ratio vs. Median Plot: The odds of performing a coronary angiography only increase significantly in the highest Troponin I quintile (non-linear association)

