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## Coronary angiography in worsening heart failure

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Table 1. Characteristics of the BIOSTAT population by Coronary Angiography Realization

	N	Global Population (n=2516)	No Coronary Angiography (n=2201)	Coronary Angiography Performed (n=315)	P-value
Age, years	2516	68.4 ± 12.0	69.1 ± 11.9	63.7 ± 11.6	<0.0001
Male gender, n (%)	2516	1846 (73.4 %)	1621 (73.6 %)	225 (71.4 %)	0.40
BMI, kg/m <sup>2</sup>	2478	27.9 ± 5.5	27.8 ± 5.4	28.2 ± 6.1	0.29
Heart rate, bpm	2497	82.3 ± 21.4	81.6 ± 21.3	87.4 ± 21.4	<0.0001
SBP, mmHg	2511	124.7 ± 21.9	124.6 ± 21.6	125.3 ± 23.8	0.63
DBP, mmHg	2511	74.9 ± 13.4	74.7 ± 13.0	76.1 ± 15.8	0.079
Pulmonary rales, n (%)	2445	1291 (52.8 %)	1101 (51.5 %)	190 (61.5 %)	0.001
Peripheral edema, n (%)	2099	1256 (59.8 %)	1106 (59.9 %)	150 (59.3 %)	0.85
Elevated JVP, n (%)	1753	554 (31.6 %)	479 (31.2 %)	75 (34.4 %)	0.34
NYHA class III/IV, n (%)	2446	1522 (62.2 %)	1324 (61.8 %)	198 (65.1 %)	0.26
Orthopnea, n (%)	2511	879 (35.0 %)	745 (33.9 %)	134 (42.5 %)	0.003
LVEF, %	2243	31.0 ± 10.6	31.4 ± 10.7	28.7 ± 9.7	<0.0001
Northern Europe, n (%)	2516	1200 (47.7%)	1035 (47.0 %)	165 (52.4 %)	0.075
Inpatient visit, n (%)	2516	1694 (67.3 %)	1389 (63.1 %)	305 (96.8 %)	<0.0001
Heart failure hospitalization within the last year, n (%)	2516	794 (31.6 %)	751 (34.1 %)	43 (13.7 %)	<0.0001
HF etiology: Ischemic, n (%)	2516	1103 (43.8 %)	988 (44.9 %)	115 (36.5 %)	0.005
HF etiology: Hypertensive, n (%)		254 (10.1 %)	225 (10.2 %)	29 (9.2 %)	
HF etiology: Valvular, n (%)		190 (7.6 %)	169 (7.7 %)	21 (6.7 %)	
HF etiology: Other/mixed, n (%)		969 (38.5 %)	819 (37.2 %)	150 (47.6 %)	
<b>Precipitating factors for index heart failure, n (%)</b>					
Acute coronary syndrome, n (%)	1703	155 (9.1 %)	101 (6.9 %)	54 (23.1 %)	<0.0001
Non-compliance, n (%)	1702	304 (17.9 %)	274 (18.7 %)	30 (12.9 %)	0.032
Atrial Fibrillation, n (%)	1703	770 (45.2 %)	691 (47.0 %)	79 (33.8 %)	0.0002
Infection, n (%)	1703	224 (13.2 %)	199 (13.5 %)	25 (10.7 %)	0.23
Uncontrolled hypertension, n (%)	1703	244 (14.3 %)	198 (13.5 %)	46 (19.7 %)	0.012
Renal dysfunction, n (%)	1703	439 (25.8 %)	403 (27.4 %)	36 (15.4 %)	<0.0001
Other/mixed, n (%)	1703	287 (16.9 %)	228 (15.5 %)	59 (25.2 %)	0.0002
Coronary stenosis, n (%)	312	122 (39.1%)	0	122 (39.1 %)	NA
<b>Comorbidities</b>					
Hypertension, n (%)	2516	1569 (62.4 %)	1381 (62.7 %)	188 (59.7 %)	0.29
Atrial Fibrillation, n (%)	2516	1143 (45.4 %)	1044 (47.4 %)	99 (31.4 %)	<0.0001
Diabetes mellitus, n (%)	2516	819 (32.6 %)	717 (32.6 %)	102 (32.4 %)	0.94
Never smoked, n (%)	2513	940 (37.4 %)	838 (38.1 %)	102 (32.5 %)	<0.0001
Past smoker, n (%)		1220 (48.5 %)	1083 (49.2 %)	137 (43.6 %)	
Current smoker, n (%)		353 (14.0 %)	278 (12.6 %)	75 (23.9 %)	
COPD, n (%)	2516	436 (17.3 %)	385 (17.5 %)	51 (16.2 %)	0.57
Stroke, n (%)	2516	233 (9.3 %)	217 (9.9 %)	16 (5.1 %)	0.006
Peripheral Artery Disease, n (%)	2516	273 (10.9 %)	245 (11.1 %)	28 (8.9 %)	0.23
Device therapy, n (%)	2516	618 (24.6 %)	591 (26.9 %)	27 (8.6 %)	<0.0001
<b>Laboratory values</b>					
Hemoglobin, g/dL	2293	13.2 ± 1.9	13.1 ± 1.9	13.5 ± 1.9	0.0009

eGFR, ml/min/1.73m <sup>2</sup>	2516	62.4 ± 23.2	61.5 ± 23.3	69.4 ± 21.7	<0.0001
Urea, mmol/L	2083	11.4 (7.6 - 18.2)	11.8 (7.8 - 18.6)	8.9 (6.5 - 15.0)	<0.0001
Sodium, mmol/L	2327	139.1 ± 4.0	139.1 ± 4.1	139.2 ± 3.7	0.92
Potassium, mmol/L	2324	4.3 ± 0.6	4.3 ± 0.6	4.2 ± 0.6	0.001
Albumin, g/L	2361	32.4 ± 8.8	32.4 ± 8.9	32.2 ± 7.9	0.75
Glucose, mmol/L	1894	7.2 ± 3.1	7.1 ± 3.1	7.3 ± 2.8	0.31
ALAT, UI/L	1804	25.0 (17.0 - 38.0)	24.0 (16.0 - 36.0)	32.0 (21.0 - 48.5)	<0.0001
ASAT, UI/L	1598	25.0 (19.0 - 35.0)	25.0 (19.0 - 34.0)	29.0 (21.0 - 41.0)	<0.0001
Gamma-GT, UI/L	1151	55.0 (28.0 - 108.2)	55.0 (28.0 - 108.0)	56.0 (28.0 - 114.0)	0.055
Total bilirubin, µmol/L	1381	14.0 (10.0 - 21.0)	15.0 (10.0 - 21.0)	11.6 (8.7 - 17.0)	0.43
HDL, mmol/L	1166	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.4	0.32
LDL, mmol/L	1103	2.6 ± 1.1	2.5 ± 1.0	2.8 ± 1.1	0.007
Total cholesterol, mmol/L	1407	4.3 ± 1.3	4.2 ± 1.3	4.5 ± 1.3	0.037
Triglycerides, mmol/L	1309	1.5 ± 1.0	1.5 ± 1.1	1.4 ± 1.0	0.74
LogNT-pro BNP, ng/L	2174	3.0 ± 1.4	3.1 ± 1.4	2.9 ± 1.2	0.10
Troponin I, pg/mL	2352	12.8 (6.8 - 27.9)	12.3 (6.7 - 25.6)	19.1 (8.1 - 36.0)	<0.0001
<b>Medication</b>					
PCI or CABG, n (%)	2516	842 (33.5 %)	774 (35.2 %)	68 (21.6 %)	<0.0001
Loop diuretic, n (%)	2516	2504 (99.5 %)	2193 (99.6 %)	311 (98.7 %)	0.081
ACEi/ARB, n (%)	2516	1820 (72.3 %)	1574 (71.5 %)	246 (78.1 %)	0.015
Beta-blocker, n (%)	2516	2093 (83.2 %)	1829 (83.1 %)	264 (83.8 %)	0.75
MRA, n (%)	2516	1339 (53.2 %)	1178 (53.5 %)	161 (51.1 %)	0.42
Digoxin, n (%)	2516	491 (19.5 %)	441 (20.0 %)	50 (15.9 %)	0.081
Death or heart failure hospitalization, n (%)	2516	1017 (40.4 %)	932 (42.3 %)	85 (27.0 %)	<0.0001
Death, n (%)	2516	657 (26.1 %)	612 (27.8 %)	45 (14.3 %)	<0.0001
Heart failure hospitalization n (%)	2516	609 (24.2 %)	559 (25.4 %)	50 (15.9 %)	0.0002

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; ALAT/ASAT, alanine and aspartate aminotransferase levels; 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. European regions were divided in Southern countries (Greece, Italy, Serbia, Slovenia, and France) vs. Northern countries (Netherlands, Sweden, Norway, Germany, Poland, and United Kingdom).



Table 2. Logistic regression for the odds of performing a coronary angiography

Variable	Odds Ratio (95%CI) for Coronary Angiography Realization	P-value
Inpatient visit (yes)	11.554 (4.636-28.794)	<0.0001
Acute coronary syndrome (yes)	3.117 (1.939-5.009)	<0.0001
Troponin I (>36 pg/mL)	1.603 (1.115-2.305)	0.011
Age (per each decade less)	1.389 (1.202-1.605)	<0.0001
eGFR (per 10 ml/min/1.73m <sup>2</sup> increase)	1.085 (1.000-1.177)	0.049
Device Therapy (yes)	0.430 (0.254-0.727)	0.002
Heart failure hospitalization within the last year (yes)	0.577 (0.371-0.897)	0.014
Previous PCI or CABG (yes)	0.614 (0.413-0.912)	0.016

Legend: CI, confidence interval; eGFR, estimated glomerular filtration rate; PCI or CABG, percutaneous coronary intervention or coronary artery bypass grafting.

Table 3. Logistic regression for the odds of having a coronary artery stenosis

Variable	Odds Ratio (95%CI) for Coronary Critical Stenosis	P-value
Ischemic Heart Failure (yes)	33.426 (16.439-67.967)	<0.0001
Troponin I (per 1 Log increase)	1.309 (1.032-1.661)	0.026

Legend: CI, confidence interval.

Table 4. Prognostic assessment of coronary angiography and presence of critical stenosis

<b>Outcome</b>	<b>Coronary angiography: unadjusted HR (95%CI)</b>	<b>P-value</b>	<b>Coronary angiography: adjusted* HR (95%CI)</b>	<b>P-value</b>
Death or HHF	0.568 (0.455-0.709)	<0.0001	0.714 (0.571-0.893) **	0.003
HHF	0.564 (0.422-0.754)	<0.0001	0.702 (0.525-0.940)	0.017
Death	0.460 (0.340-0.623)	<0.0001	0.586 (0.433-0.795) **	0.001
<b>Outcome</b>	<b>Coronary stenosis: unadjusted HR (95%CI)</b>	<b>P-value</b>	<b>Coronary stenosis: adjusted* HR (95%CI)</b>	<b>P-value</b>
Death or HHF	1.940 (1.261-2.985)	0.003	1.705 (1.103-2.635)	0.016
HHF	1.583 (0.903-2.776)	0.109	1.465 (0.833-2.575)	0.185
Death	2.716 (1.473-5.009)	0.001	2.089 (1.103-3.957)	0.024

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

\*model adjusted on age, 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 calculator (<https://biostat-chf.shinyapps.io/calc/>).

P for interaction HF etiology\*Coronary Angiography =0.007 for the primary outcome of death or HHF; P =0.004 for death; and non-significant for HHF, P =0.326.

\*\*HR (95%CI) results for Coronary Angiography adjusted on the above models plus Heart Failure Etiology (ischemic vs. other) plus the interaction between Heart Failure Etiology and Coronary Angiography: Death or HHF =0.553 (0.402-0.761), p <0.0001; Death =0.378 (0.235-0.609), p <0.0001.

Further adjustment on the type of centre: 1) university hospital, 2) large non-academic centre, and 3) small centre, provided overlapping results to those presented in the table.

