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**Circulating plasma concentrations of ACE2 in men and women with heart failure and effects of renin-angiotensin-aldosterone-inhibitors**

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1 **Supplemental Table 1:** Baseline characteristics according to quartiles of plasma ACE concentrations (validation cohort)

	Q1[2.60,4.83) <i>N=423</i>	Q2[4.83,5.26) <i>N=422</i>	Q3[5.26,5.79) <i>N=425</i>	Q4[5.79,8.46] <i>N=421</i>	p-value	N
<b>validation Cohort</b>						
ACE2 plasma concentrations (NPX)	4.56 [4.34;4.72]	5.06 [4.95;5.17]	5.50 [5.38;5.63]	6.27 [6.01;6.62]	0.000	1691
Sex:					<0.001	1691
Men	222 (52.5%)	266 (63.0%)	308 (72.5%)	321 (76.2%)		
Women	201 (47.5%)	156 (37.0%)	117 (27.5%)	100 (23.8%)		
Age (years)	74.0 [66.0;80.0]	76.0 [67.0;82.0]	75.0 [67.0;82.0]	75.0 [67.0;82.0]	0.040	1691
Body mass index (kg/m <sup>2</sup> )	28.4 [24.9;33.3]	27.7 [24.6;32.4]	28.0 [24.2;32.3]	28.1 [24.5;32.7]	0.417	1657

	Q1[2.60,4.83)	Q2[4.83,5.26)	Q3[5.26,5.79)	Q4[5.79,8.46]	p-value	N
	<i>N=423</i>	<i>N=422</i>	<i>N=425</i>	<i>N=421</i>		
Heart rate (beats/minute)	70.0 [60.0;81.0]	71.0 [62.0;84.0]	72.0 [63.0;84.0]	75.0 [64.0;88.0]	<0.001	1653
Systolic blood pressure (mmHg)	125 [111;142]	124 [110;143]	122 [110;139]	121 [107;137]	0.044	1663
Left ventricular ejection fraction	42.0 [35.0;51.0]	40.0 [35.0;50.0]	40.0 [35.0;50.0]	39.0 [30.0;50.0]	0.026	1530
New York Heart Association (NYHA) class:					.	1690
Class I	7 (1.66%)	4 (0.95%)	4 (0.94%)	1 (0.24%)		
Class II	203 (48.1%)	174 (41.2%)	164 (38.6%)	155 (36.8%)		
Class III	173 (41.0%)	178 (42.2%)	197 (46.4%)	204 (48.5%)		
Class IV	39 (9.24%)	66 (15.6%)	60 (14.1%)	61 (14.5%)		

	Q1[2.60,4.83)	Q2[4.83,5.26)	Q3[5.26,5.79)	Q4[5.79,8.46]	p-value	N
	<i>N=423</i>	<i>N=422</i>	<i>N=425</i>	<i>N=421</i>		
History of Atrial fibrillation	163 (38.8%)	179 (42.6%)	188 (44.8%)	214 (51.3%)	0.003	1677
Renal disease	174 (42.0%)	190 (45.6%)	198 (47.0%)	202 (48.4%)	0.283	1669
Diabetes	98 (23.4%)	134 (31.8%)	149 (35.3%)	166 (39.6%)	<0.001	1682
Hypertension	237 (56.2%)	252 (59.9%)	252 (60.0%)	244 (58.0%)	0.635	1684
Chronic obstructive pulmonary disease	73 (17.4%)	78 (18.6%)	79 (18.7%)	77 (18.6%)	0.955	1677
Myocardial infarction	185 (43.8%)	215 (51.2%)	219 (51.7%)	205 (48.7%)	0.090	1687
Ischemic HF aetiology	250 (95.1%)	290 (95.7%)	280 (91.8%)	275 (94.8%)	0.165	1161

	Q1[2.60,4.83]	Q2[4.83,5.26]	Q3[5.26,5.79]	Q4[5.79,8.46]	p-value	N
	N=423	N=422	N=425	N=421		
Coronary artery disease	204 (48.6%)	237 (56.3%)	250 (59.4%)	230 (54.8%)	0.015	1682
Coronary artery by-pass graft	59 (13.9%)	65 (15.4%)	79 (18.6%)	92 (21.9%)	0.012	1689
Percutaneous coronary intervention	70 (16.7%)	87 (20.7%)	74 (17.7%)	81 (19.4%)	0.464	1674
Use of Angiotensin Converting Enzyme (ACE) inhibitor or Angiotensin Receptor Blocker (ARB)	319 (75.4%)	308 (73.0%)	299 (70.4%)	269 (63.9%)	0.002	1691
Beta-blockers	317 (74.9%)	305 (72.3%)	306 (72.0%)	296 (70.3%)	0.508	1691
ACE inhibitors	237 (56.0%)	236 (55.9%)	218 (51.3%)	196 (46.6%)	0.016	1691
ARBs	82 (19.4%)	76 (18.0%)	83 (19.5%)	74 (17.6%)	0.849	1691
Mineralocorticoid Receptor Antagonist (MRA)	114 (27.0%)	142 (33.6%)	144 (33.9%)	145 (34.4%)	0.064	1691
ACE inhibitors and MRA:					0.016	1691

	Q1[2.60,4.83)	Q2[4.83,5.26)	Q3[5.26,5.79)	Q4[5.79,8.46]	p-value	N
	<i>N=423</i>	<i>N=422</i>	<i>N=425</i>	<i>N=421</i>		
ACEi with MRA	71 (16.8%)	93 (22.0%)	84 (19.8%)	74 (17.6%)		
ACEi without MRA	166 (39.2%)	143 (33.9%)	134 (31.5%)	122 (29.0%)		
MRA without ACEi	43 (10.2%)	49 (11.6%)	60 (14.1%)	71 (16.9%)		
no ACEi and no MRA	143 (33.8%)	137 (32.5%)	147 (34.6%)	154 (36.6%)		