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

| | Q1[2.78,4.80) | Q2[4.80,5.25) | Q3[5.25,5.76) | Q4[5.76,8.72] | p-value | N |
|--------------------------------------|---------------------|---------------------|---------------------|---------------------|---------|------|
| | <i>N=506</i> | <i>N=505</i> | <i>N=506</i> | <i>N=505</i> | | |
| Index Cohort | | | | | | |
| ACE2 plasma concentrations (NPX) | 4.49 [4.25;4.65] | 5.03 [4.92;5.14] | 5.48 [5.35;5.62] | 6.17 [5.97;6.52] | 0.000 | 2022 |
| Sex: | | | | | <0.001 | 2022 |
| Men | 329 (65.0%) | 353 (69.9%) | 381 (75.3%) | 422 (83.6%) | | |
| Women | 177 (35.0%) | 152 (30.1%) | 125 (24.7%) | 83 (16.4%) | | |
| Age (years) | 69.0 [61.0;77.0] | 71.0 [62.0;79.0] | 71.0 [62.0;78.0] | 70.0 [61.0;78.0] | 0.394 | 2022 |
| Body mass index (kg/m ²) | 27.2 [24.5;31.1] | 27.1 [24.0;30.9] | 26.6 [23.8;29.8] | 27.2 [24.2;31.0] | 0.148 | 1990 |
| Heart rate (beats/minute) | 74.0 [65.0;84.0] | 76.0 [68.0;90.0] | 77.0 [67.0;90.0] | 78.0 [69.0;90.0] | <0.001 | 2017 |

| | Q1[2.78,4.80) | Q2[4.80,5.25) | Q3[5.25,5.76) | Q4[5.76,8.72] | p-value | N |
|--|---------------------|---------------------|---------------------|---------------------|---------|------|
| | <i>N=506</i> | <i>N=505</i> | <i>N=506</i> | <i>N=505</i> | | |
| Systolic blood pressure (mmHg) | 125 [110;140] | 121 [110;140] | 120 [110;136] | 120 [108;132] | <0.001 | 2018 |
| Left ventricular ejection fraction | 30.0 [25.0;38.0] | 30.0 [25.0;36.0] | 30.0 [24.0;37.0] | 30.0 [23.0;35.0] | <0.001 | 1804 |
| New York Heart Association (NYHA) class: | | | | | <0.001 | 1961 |
| I | 17 (3.44%) | 11 (2.25%) | 11 (2.23%) | 3 (0.62%) | | |
| II | 216 (43.7%) | 198 (40.5%) | 164 (33.3%) | 138 (28.5%) | | |
| III | 214 (43.3%) | 230 (47.0%) | 239 (48.5%) | 278 (57.3%) | | |
| IV | 47 (9.51%) | 50 (10.2%) | 79 (16.0%) | 66 (13.6%) | | |
| History of Atrial fibrillation | 196 (38.7%) | 197 (39.0%) | 242 (47.8%) | 283 (56.0%) | <0.001 | 2022 |
| Renal disease | 136 (26.9%) | 133 (26.3%) | 145 (28.7%) | 161 (31.9%) | 0.199 | 2022 |
| Diabetes | 160 (31.6%) | 169 (33.5%) | 150 (29.6%) | 166 (32.9%) | 0.574 | 2022 |
| Hypertension | 330 (65.2%) | 308 (61.0%) | 322 (63.6%) | 286 (56.6%) | 0.029 | 2022 |

| | Q1[2.78,4.80) | Q2[4.80,5.25) | Q3[5.25,5.76) | Q4[5.76,8.72] | p-value | N |
|---|---------------|---------------|---------------|---------------|---------|------|
| | <i>N=506</i> | <i>N=505</i> | <i>N=506</i> | <i>N=505</i> | | |
| Chronic obstructive pulmonary disease | 99 (19.6%) | 92 (18.2%) | 76 (15.0%) | 79 (15.6%) | 0.178 | 2022 |
| Myocardial infarction | 184 (36.4%) | 199 (39.4%) | 173 (34.2%) | 197 (39.0%) | 0.276 | 2022 |
| Ischemic HF etiology | 257 (51.7%) | 275 (55.6%) | 260 (52.8%) | 290 (58.1%) | 0.175 | 1983 |
| Coronary artery disease | 211 (41.7%) | 232 (45.9%) | 205 (40.5%) | 245 (48.5%) | 0.037 | 2022 |
| Coronary artery by-pass graft | 73 (14.4%) | 85 (16.8%) | 73 (14.4%) | 117 (23.2%) | <0.001 | 2022 |
| Percutaneous coronary intervention | 101 (20.0%) | 110 (21.8%) | 98 (19.4%) | 112 (22.2%) | 0.632 | 2022 |
| Use of Angiotensin Converting Enzyme (ACE) inhibitor or Angiotensin Receptor Blocker (ARB) | 374 (73.9%) | 365 (72.3%) | 351 (69.4%) | 366 (72.5%) | 0.434 | 2022 |
| Beta-blockers | 427 (84.4%) | 423 (83.8%) | 407 (80.4%) | 423 (83.8%) | 0.325 | 2022 |
| ACE inhibitors | 304 (60.1%) | 315 (62.4%) | 310 (61.3%) | 315 (62.4%) | 0.857 | 2022 |
| ARBs | 72 (14.2%) | 59 (11.7%) | 49 (9.68%) | 56 (11.1%) | 0.150 | 2022 |
| Mineralocorticoid Receptor Antagonist (MRA) | 256 (50.6%) | 249 (49.3%) | 259 (51.2%) | 299 (59.2%) | 0.007 | 2022 |
| ACE inhibitors and MRA: | | | | | 0.043 | 2022 |

| | Q1[2.78,4.80] | Q2[4.80,5.25) | Q3[5.25,5.76) | Q4[5.76,8.72] | p-value | N |
|-----------------------|---------------|---------------|---------------|---------------|---------|---|
| | <i>N=506</i> | <i>N=505</i> | <i>N=506</i> | <i>N=505</i> | | |
| ACEi with MRA | 154 (30.4%) | 168 (33.3%) | 172 (34.0%) | 189 (37.4%) | | |
| ACEi without MRA | 150 (29.6%) | 147 (29.1%) | 138 (27.3%) | 126 (25.0%) | | |
| MRA without ACEi | 102 (20.2%) | 81 (16.0%) | 87 (17.2%) | 110 (21.8%) | | |
| no ACEi and no MRA | 100 (19.8%) | 109 (21.6%) | 109 (21.5%) | 80 (15.8%) | | |