**Supplementary Table 1.** Demographic, clinical and functional characteristics according to presence of depressed baroreceptor sensitivity (BRS <3 ms/mm Hg)

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **BRS < 3 ms/mm Hg**  **(n 124)** | **BRS > 3**  **ms/mm Hg**  **(n 123)** | **P value** |
| Age (years) | 55 (49-61) | 54 (48-57) | 0.03 |
| Male Sex (%) | 87 | 82 | 0.28 |
| NYHA Class (%) |  |  | <0.001 |
| I-II | 39 | 88 |  |
| III-IV | 61 | 12 |  |
| Cause of Heart Failure (%): |  |  | 0.02 |
| Ischemic | 58 | 43 |  |
| Non-ischemic | 42 | 57 |  |
| Baseline RR interval (ms) | 826 (703-910) | 935 (839-1038) | <0.001 |
| Resting Systolic Arterial Pressure (mmHg) | 110 (100-120) | 115 (110-130) | <0.001 |
| Resting Diastolic Arterial Pressure (mmHg) | 70 (70-80) | 70 (70-80) | 0.004 |
| Left ventricular ejection fraction (%) | 25 (21-29) | 31 (25-36) | <0.001 |
| Left ventricular end systolic diameter (mm) | 61 (55-69) | 54 (48-62) | <0.001 |
| Left ventricular end diastolic diameter (mm) | 71 (66-80) | 67 (62-72) | <0.001 |
| Mitral regurgitation 2 -3+, (%) | 43 | 15 | <0.001 |
| Peak VO2 ml/kg/min | 14 (11-16) | 17 (14-20) | <0.001 |
| Ventricular premature contractions (n/hour) |  |  |  |
| Non-sustained ventricular tachycardia (%) | 18 (6-81) | 9 (2-50) | 0.004 |
| SDNN (ms) | 41 | 34 | 0.26 |
| Baroreceptor Sensitivity (ms/mm Hg) | 1.0 (0.10 -2.0) | 7.4 (4.9 -11.0) | <0.001 |
| Angiotensin converting enzyme inhibitor (%) | 83 | 89 | 0.16 |
| Beta-blocker (%) | 26 | 58 | <0.001 |
| Diuretics (%) | 90 | 84 | 0.12 |
| Nitrates (%) | 59 | 48 | 0.09 |
| Digitalis (%) | 62 | 47 | 0.02 |
| Amiodarone (%) | 29 | 26 | 0.60 |
| Blood urea nitrogen (mg/dL) | 52 (46-55) | 44 (37-52) | <0.001 |
| Creatinine (mg/dL) | 1.21 (1.08-1.39) | 1.10 (0.97-1.23) | <0.001 |
| eGFR (ml/min/1.73m2) | 65 (54-76) | 73 (64-87) | <0.001 |
| Sodium (mEq/L) | 140 (138-141) | 141 (139-142) | 0.001 |
| Potassium (mEq/L) | 4.4 (4.2-4.7) | 4.3 (4.1-4.5) | 0.004 |

ms/mmHG=milliseconds/millimeter of mercury. Continuous variables are expressed as median (interquartile range). NYHA=New York Heart Association. LVEF= left ventricular ejection fraction. SDNN = standard deviation of normal-to-normal RR intervals. Ms = milliseconds. mEq/L=milliequivalent/liter. mg/dL=milligram/decilitre. BRS-baroreceptor sensitivity. VO2=volume of oxygen consumption. eGFR=estimated glomerular filtration rate.

**Supplementary Table 2.** Demographic, clinical and functional characteristics according to CKD and baro-receptor sensitivity

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **BRS**  **<3 ms/mm Hg** | | | **BRS**  **≥3 ms/mm Hg** | | |
| **Characteristic** | **CKD**  (n=41) | **Preserved Kidney Function**  (n=83) | **P value** | **CKD**  (n=27) | **Preserved Kidney Function**  (n=96) | **P value** |
| Age (years) | 60 (52-63) | 52 (46-59) | <0.001 | 56 (54-60) | 53 (46-57) | 0.001 |
| Sex (% male) | 88 | 87 | 0.869 | 78 | 83 | 0.51 |
|  |  |  |  |  |  |  |
| NYHA Class (%) |  |  | 0.26 |  |  | 0.26 |
| I-II | 32 | 42 |  | 81 | 90 |  |
| III-IV | 68 | 58 |  | 19 | 10 |  |
| Cause of CHF (%): |  |  | 0.04 |  |  | 0.02 |
| Ischemic | 71 | 52 |  | 63 | 38 |  |
| Non-ischemic | 29 | 48 |  | 37 | 62 |  |
|  |  |  |  |  |  |  |
| Baseline RR interval (ms) | 828 (742-909) | 824 (681-919) | 0.47 | 940 (817-1038) | 935 (841-1040) | 0.97 |
| Resting Systolic Arterial Pressure (mmHg) | 110 (100-125) | 110 (100-120) | 0.21 | 120 (110-120) | 110 (110-130) | 0.49 |
| Resting Diastolic Arterial Pressure (mmHg) | 70 (70-80) | 70 (70-75) | 0.50 | 80 (70-80) | 70 (70-80) | 0.20 |
|  |  |  |  |  |  |  |
| Left ventricular ejection fraction (%) | 25 (21-30) | 26 (21-29) | 0.97 | 27 (23-37) | 31 (25-36) | 0.23 |
| Left ventricular end systolic diameter (mm) | 61 (52-66) | 61 (56-62) | 0.17 | 56 (48-62) | 54 (49-62) | 0.664 |
| Left ventricular end diastolic diameter (mm) | 70 (63-72) | 72 (67-81) | 0.07 | 67 (61-71) | 68 (62-73) | 0.41 |
| Mitral regurgitation 2 -3+, (%) | 34 | 47 | 0.17 | 22 | 13 | 0.21 |
|  |  |  |  |  |  |  |
| Peak VO2 ml/kg/min | 12 (11-14) | 15 (12-17) | 0.001 | 15 (12-17) | 17 (15-21) | 0.01 |
|  |  |  |  |  |  |  |
| Ventricular premature contractions (n/hour) | 18 (6-61) | 20 (5-84) | 0.79 | 13 (2-51) | 9 (2-48) | 0.78 |
| Non-sustained ventricular tachycardia (%) | 32 | 46 | 0.13 | 37 | 33 | 0.72 |
| SDNN (ms) | 76 (61-99) | 74 (48-101) | 0.54 | 94 (63-114) | 106 (83-128) | 0.08 |
| Baroreceptor Sensitivity (ms/mmm Hg) | 0.9 (0.1 -1.8) | 1.0 (0.1 -2.0) | 0.69 | 7.0 (4.7-10.0) | 7.5 (5.0 -11.1) | 0.50 |
|  |  |  |  |  |  |  |
| Angiotensin converting enzyme inhibitor (%) | 80 | 83 | 0.13 | 96 | 88 | 0.16 |
| Beta-blocker (%) | 27 | 25 | 0.86 | 52 | 59 | 0.86 |
| Diuretics (%) | 88 | 92 | 0.51 | 96 | 80 | 0.03 |
| Nitrates (%) | 71 | 53 | 0.06 | 70 | 42 | 0.01 |
| Digitalis (%) | 63 | 61 | 0.83 | 67 | 42 | 0.02 |
| Amiodarone (%) | 44 | 22 | 0.01 | 41 | 22 | 0.05 |
| Blood urea nitrogen (mg/dl) | 70 (54-88) | 50 (43-55) | <0.001 | 54 (50-60) | 41 (35-46) | <0.001 |
| Creatinine (mg/dl) | 1.48 (1.39-1.70) | 1.14 (1.00-1.23) | <0.001 | 1.40 (1.32-1.49) | 1.06 (0.92-1.15) | <0.001 |
| eGFR (mL/min/1.73m2) | 49 (42-53) | 72 (65-81) | <0.001 | 53 (50-57) | 79 (70-90) | <0.001 |
| Sodium (mEq/L) | 140 (137-141) | 140 (138-141) | 0.27 | 141 (139-143) | 141 (139-142) | 0.90 |

ms/mmHG=milliseconds/millimeter of mercury. Continuous variables are expressed as median (interquartile range). NYHA=New York Heart Association. LVEF= left ventricular ejection fraction. SDNN = standard deviation of normal-to-normal RR intervals. Ms = milliseconds. mEq/L=milliequivalent/liter. mg/dL=milligram/decilitre. BRS-baroreceptor sensitivity. VO2=volume of oxygen consumption. eGFR=estimated glomerular filtration rate.

**Supplementary Figure**. Theoretical model and assumptions in the study regarding the pathophysiology of CKD and BRS in heart failure

Diagram

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