**Supplemental Figure 1.** **e′VM algorithm**

Diagram

Description automatically generated

**Supplemental Table 1.** **Age-specific limits for e**' **mean, LVEDVi and LVMi**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **e′ mean (cm/sec)** | **LVEDVi (ml/m²)** | **LVMi (g/m²)** | **LVMi2 (g/m²)** |
| **40 years** | 12 | 56 | 72 | 97 |
| **50 years** | 11 | 53 | 76 | 101 |
| **60 years (reference)** | 10 | 50 | 80 | 105 |
| **70 years** | 9 | 47 | 84 | 109 |
| **80 years** | 8 | 44 | 88 | 113 |

Reference limits at 60 years of age were defined by original thresholds of the e'VM algorithm, while age-specific cut-off values were determined according to previous reports 16, 17.

**Supplemental Table 2. Change in echocardiographic and biomarker variables in response to spironolactone across the e**'**VM phenotype strata**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **MN phenotype** | | | | **D phenotype** | | | | **D/S phenotype** | | | |
|  | **Spironolactone** | **placebo** | **mean ± SD** | **adj-p** | **Spironolactone** | **placebo** | **mean ± SD** | **adj-p** | **Spironolactone** | **placebo** | **mean ± SD** | **adj-p** |
| **LVEDVi**  **change, ml/m²** | -0.6 ± 5.5 | -1.0 ± 5.2 | 0.4 ± 1.5 | 0.87 | -1.2 ± 4.5 | -1.0 ± 4.4 | -0.2 ± 0.6 | 0.95 | -1.8 ± 5.2 | -1.6 ± 5.3 | -0.4 ± 0.9 | 0.71 |
| **LVMi change,**  **g/m²** | -0.7 ± 15.4 | 0.1 ± 9.6 | -0.4 ± 3.4 | 0.65 | -0.5 ± 8.9 | 0.7 ± 10.4 | -1.2 ± 1.4 | 0.32 | -6.7 ± 13.9 | -0.9 ± 14.7 | -6.4 ± 2.7 | **0.012** |
| **LAVi change,**  **ml/m²** | -3.3 ± 8.4 | -1.2 ± 4.6 | -1.8 ± 1.6 | 0.29 | -1.0 ± 5.0 | -0.9 ± 6.2 | -0.2 ± 0.7 | 0.70 | -2.1 ± 5.2 | -0.0 ± 5.3 | -2.3 ± 1 | **0.028** |
| **E/e’ change,**  **/unit** | 0.1 ± 2.2 | 0.9 ± 1.5 | -0.7 ± 0.5 | **0.04** | -0.3 ± 2.1 | -0.4 ± 2.4 | 0.2 ± 0.3 | 0.70 | -1.0 ± 2.5 | 0.0 ± 3.2 | -1.5 ± 0.5 | **0.004** |
| **SBP change,**  **mmHg** | -9.1 ± 15.4 | 0.2 ± 14.3 | -12.2 ± 3.1 | **0.002** | -13.0 ± 19.8 | -3.5 ± 18.5 | -8.3 ± 2.2 | **0.002** | -15.9 ± 17.0 | -7.0 ± 21.8 | -10.7 ± 3 | **<0.001** |
| **PIIINP change,**  **µg/L** | -0.1 ± 2.2 | -0.2 ± 1.4 | 0.1 ± 0.5 | 0.63 | -0.0 ± 1.7 | -0.3 ± 1.7 | 0 ± 0.2 | 0.93 | -0.2 ± 1.7 | -0.3 ± 2.3 | -0.2 ± 0.3 | 0.45 |
| **PICP change,**  **µg/L** | -9.0 ± 24.8 | 1.5 ± 19.6 | -6.9 ± 4.6 | 0.12 | -6.6 ± 26.5 | -1.9 ± 18.5 | -6.3 ± 3 | **0.032** | -9.9 ± 22.9 | 0.2 ± 26.3 | -12.6 ± 4 | **0.003** |
| **NTproBNP**  **change, µg/L** | -8.0 ± 179.3 | 68.5 ± 202.5 | -23.5 ± 49.3 | 0.64 | -25.4 ± 163.5 | -10.4 ± 196.9 | -17.9 ± 21.9 | 0.33 | -18.9 ± 155.4 | 119.3 ± 613.6 | -134.2 ± 84.9 | 0.06 |
| **BNP change** | -0.1 ± 1.2 | 0.5 ± 1.1 | -0.4 ± 0.3 | 0.15 | -0.0 ± 1.0 | -0.1 ± 0.9 | 0 ± 0.1 | 0.67 | -0.3 ± 1.0 | 0.3 ± 1.0 | -0.6 ± 0.2 | **0.002** |

\* Adjusted for age, sex, body mass index, a prevalence of hypertension, diabetes mellitus, glomerular filtration rate and baseline echocardiographic/proteomic variables.

\*\*Echocardiographic and biomarker variables were assessed by changes from baseline to month 9.