

SUPPLEMENTAL MATERIAL: Relations of Insulin Resistance and Glycemic Abnormalities to Cardiovascular Magnetic Resonance Measures of Cardiac Structure and Function: the Framingham Heart Study

I. Relations of HOMA-IR (as a continuous variable) to CMR measures

II. Relations of 2-hr insulin to CMR measures

III. Relations of 2-hr glucose to CMR measures

IV. Relations of HOMA-IR to LVM and LVEDV separately

V. Relations of glycemia categories to LVM and LVEDV separately

Supplementary Table 1: Relations of HOMA-IR to CMR measures

| | Model | Beta estimate (SE)* | p-value |
|--|--------------|----------------------------|----------------|
| MEN | | | |
| LAD, mm | Age-adjusted | 1.03 (0.31) | 0.0008 |
| | MV-adjusted | -0.97 (0.32) | 0.002 |
| LVM/ht^{2.7}, g/m^{2.7} | Age-adjusted | 1.76 (0.33) | <0.0001 |
| | MV-adjusted | -0.31 (0.34) | 0.36 |
| LVM/LVEDV, gm/ml | Age-adjusted | 0.07 (0.01) | <0.0001 |
| | MV-adjusted | 0.05 (0.01) | <0.0001 |
| RWT | Age-adjusted | 0.02 (0.003) | <0.0001 |
| | MV-adjusted | 0.01 (0.003) | 0.004 |
| CO, L/min | Age-adjusted | 0.24 (0.07) | 0.001 |
| | MV-adjusted | -0.07 (0.08) | 0.35 |
| LVEF (%) | Age-adjusted | 1.31 (0.41) | 0.002 |
| | MV-adjusted | 1.01 (0.47) | 0.03 |
| WOMEN | | | |
| LAD, mm | Age-adjusted | 1.66 (0.23) | <0.0001 |
| | MV-adjusted | -0.32 (0.23) | 0.18 |
| LVM/ht^{2.7}, g/m^{2.7} | Age-adjusted | 1.48 (0.23) | <0.0001 |
| | MV-adjusted | -0.55 (0.23) | 0.01 |
| LVM/LVEDV, gm/ml | Age-adjusted | 0.03 (0.01) | <0.0001 |
| | MV-adjusted | 0.01 (0.01) | 0.03 |
| RWT | Age-adjusted | 0.007 (0.003) | 0.007 |
| | MV-adjusted | 0.002 (0.003) | 0.44 |
| CO, L/min | Age-adjusted | 0.32 (0.05) | <0.0001 |
| | MV-adjusted | -0.03 (0.05) | 0.56 |
| LVEF (%) | Age-adjusted | 0.79 (0.29) | 0.007 |
| | MV-adjusted | 0.58 (0.34) | 0.09 |

*Cells present beta coefficient estimates (standard error) for change in CMR measures (in their units) per standard deviation change in HOMA-IR.

MV-adjusted = multivariable-adjusted; CO = cardiac output; LAD = left atrial dimension; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; LVM = left ventricular mass; RWT = relative wall thickness

MV model adjusted for age, body mass index, systolic blood pressure, cardioactive drug therapy and smoking status.

Supplementary Table 2: Adjusted CMR measures across 2-hr insulin quartiles

| Men | | | | | | |
|--|---------------|----------------------------|----------------------------|----------------------------|----------------------------|-----------------|
| | Models | Quartile 1 (n = 66) | Quartile 2 (n = 64) | Quartile 3 (n = 63) | Quartile 4 (n = 62) | p-value* |
| LAD, mm | Age-adjusted | 31 | 32 | 32 | 32 | 0.57 |
| | MV-adjusted | 32 | 32 | 32 | 30 | 0.65 |
| LVM/ht^{2.7}, g/m^{2.7} | Age-adjusted | 27.6 | 27.9 | 27.0 | 29.1 | 0.22 |
| | MV-adjusted | 29.0 | 28.2 | 27.0 | 27.2 | 0.44 |
| LVM/LVEDV, gm/ml | Age-adjusted | 0.86 | 0.87 | 0.87 | 0.97 | 0.0003 |
| | MV-adjusted | 0.88 | 0.88 | 0.87 | 0.95 | 0.03 |
| RWT | Age-adjusted | 0.27 | 0.28 | 0.28 | 0.30 | 0.002 |
| | MV-adjusted | 0.28 | 0.28 | 0.28 | 0.29 | 0.30 |
| CO, L/min | Age-adjusted | 5.8 | 5.8 | 5.8 | 6.0 | 0.28 |
| | MV-adjusted | 6.0 | 5.8 | 5.8 | 5.7 | 0.08 |
| LVEF (%) | Age-adjusted | 66 | 66 | 66 | 69 | 0.04 |
| | MV-adjusted | 66 | 66 | 66 | 68 | 0.64 |
| Women | | | | | | |
| | Models | Quartile 1 (n = 72) | Quartile 2 (n = 74) | Quartile 3 (n = 74) | Quartile 4 (n = 69) | p-value* |
| LAD, mm | Age-adjusted | 27 | 28 | 28 | 30 | 0.0005 |
| | MV-adjusted | 28 | 29 | 28 | 28 | 0.13 |
| LVM/ht^{2.7}, g/m^{2.7} | Age-adjusted | 22.3 | 22.9 | 23.6 | 25.7 | <0.0001 |
| | MV-adjusted | 23.9 | 23.8 | 23.2 | 23.4 | 0.56 |
| LVM/LVEDV, gm/ml | Age-adjusted | 0.75 | 0.79 | 0.81 | 0.83 | <0.0001 |
| | MV-adjusted | 0.77 | 0.80 | 0.80 | 0.81 | 0.27 |
| RWT | Age-adjusted | 0.24 | 0.26 | 0.26 | 0.26 | 0.08 |
| | MV-adjusted | 0.25 | 0.26 | 0.26 | 0.25 | 0.77 |
| CO, L/min | Age-adjusted | 4.7 | 4.7 | 4.9 | 5.1 | 0.008 |
| | MV-adjusted | 4.9 | 4.9 | 4.9 | 4.6 | 0.80 |
| LVEF (%) | Age-adjusted | 67 | 69 | 71 | 71 | <0.0001 |
| | MV-adjusted | 67 | 69 | 71 | 71 | 0.56 |

Cells present mean values of cardiac measures; *p-value for trend.

MV-adjusted = multivariable-adjusted; CO = cardiac output; LAD = left atrial dimension; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; LVM = left ventricular mass; RWT = relative wall thickness

MV model adjusted for age, body mass index, systolic blood pressure, cardioactive drug therapy and smoking status.

Supplementary Table 3: Adjusted CMR measures across 2-hr glucose quartiles

| Men | | | | | | |
|--|---------------|----------------------------|----------------------------|----------------------------|----------------------------|-----------------|
| | Models | Quartile 1 (n = 67) | Quartile 2 (n = 67) | Quartile 3 (n = 63) | Quartile 4 (n = 58) | p-value* |
| LAD, mm | Age-adjusted | 31 | 32 | 32 | 32 | 0.13 |
| | MV-adjusted | 31 | 32 | 32 | 31 | 0.55 |
| LVM/ht^{2.7}, g/m^{2.7} | Age-adjusted | 26.9 | 27.9 | 27.8 | 28.9 | 0.07 |
| | MV-adjusted | 28.2 | 28.1 | 27.4 | 27.7 | 0.79 |
| LVM/LVEDV, gm/ml | Age-adjusted | 0.87 | 0.88 | 0.88 | 0.94 | 0.048 |
| | MV-adjusted | 0.89 | 0.89 | 0.87 | 0.91 | 0.58 |
| RWT | Age-adjusted | 0.27 | 0.28 | 0.28 | 0.30 | 0.02 |
| | MV-adjusted | 0.28 | 0.28 | 0.28 | 0.29 | 0.39 |
| CO, L/min | Age-adjusted | 5.5 | 5.8 | 6.0 | 6.1 | 0.002 |
| | MV-adjusted | 5.7 | 5.8 | 6.0 | 6.0 | 0.28 |
| LVEF (%) | Age-adjusted | 66 | 65 | 67 | 68 | 0.20 |
| | MV-adjusted | 67 | 65 | 66 | 67 | 0.38 |
| Women | | | | | | |
| | Models | Quartile 1 (n = 73) | Quartile 2 (n = 77) | Quartile 3 (n = 75) | Quartile 4 (n = 65) | p-value* |
| LAD, mm | Age-adjusted | 27 | 28 | 30 | 30 | <0.0001 |
| | MV-adjusted | 28 | 28 | 29 | 29 | 0.32 |
| LVM/ht^{2.7}, g/m^{2.7} | Age-adjusted | 21.3 | 23.0 | 25.2 | 25.0 | <0.0001 |
| | MV-adjusted | 23.2 | 23.5 | 24.1 | 23.5 | 0.60 |
| LVM/LVEDV, gm/ml | Age-adjusted | 0.75 | 0.79 | 0.82 | 0.82 | 0.0003 |
| | MV-adjusted | 0.78 | 0.80 | 0.80 | 0.80 | 0.53 |
| RWT | Age-adjusted | 0.24 | 0.27 | 0.26 | 0.26 | 0.13 |
| | MV-adjusted | 0.25 | 0.27 | 0.26 | 0.25 | 0.03 |
| CO, L/min | Age-adjusted | 4.5 | 4.8 | 5.0 | 5.0 | 0.0007 |
| | MV-adjusted | 4.8 | 4.9 | 4.8 | 4.8 | 0.80 |
| LVEF (%) | Age-adjusted | 69 | 69 | 70 | 70 | 0.20 |
| | MV-adjusted | 70 | 69 | 70 | 69 | 0.86 |

Cells present mean values of cardiac measures; *p-value for trend.

MV-adjusted = multivariable-adjusted; CO = cardiac output; LAD = left atrial dimension; LVEF = left ventricular ejection fraction; LVEDV = left ventricular end-diastolic volume; LVM = left ventricular mass; RWT = relative wall thickness

MV model adjusted for age, body mass index, systolic blood pressure, cardioactive drug therapy and smoking status.

Supplementary Table 4: Adjusted LVM and LVEDV measures across HOMA-IR quartiles

| Men | | | | | | |
|------------------|---------------|--|--|--|---|-----------------|
| | Models | Quartile 1 0.41-2.43† (n = 176) | Quartile 2 2.44-3.55† (n = 174) | Quartile 3 3.56-5.64† (n = 168) | Quartile 4 5.66-57.31† (n = 132) | p-value* |
| LVM, gm | Age-adjusted | 124 | 125 | 126 | 134 | 0.005 |
| | MV-adjusted | 131 | 127 | 124 | 126 | 0.04 |
| LVEDV, ml | Age-adjusted | 149 | 143 | 144 | 141 | 0.07 |
| | MV-adjusted | 153 | 144 | 142 | 135 | <0.0001 |
| Women | | | | | | |
| | Models | Quartile 1 0.23-2.03† (n = 216) | Quartile 2 2.04-2.84† (n = 213) | Quartile 3 2.85-4.25† (n = 208) | Quartile 4 4.26-43.01† (n = 175) | p-value* |
| LVM, gm | Age-adjusted | 82 | 82 | 86 | 93 | <0.0001 |
| | MV-adjusted | 87 | 84 | 85 | 85 | 0.20 |
| LVEDV, ml | Age-adjusted | 108 | 106 | 108 | 113 | 0.002 |
| | MV-adjusted | 112 | 108 | 108 | 105 | 0.008 |

Cells present adjusted mean values of cardiac measures; *p-value for trend; †range of HOMA-IR for the respective quartile.

MV-adjusted = multivariable-adjusted; LVM = left ventricular mass; LVEDV = left ventricular end-diastolic volume.

MV model adjusted for age, body mass index, systolic blood pressure, cardioactive drug therapy and smoking status.

Supplementary Table 5: Adjusted LVM and LVEDV measures across glycemia categories

| Men | | | | | | |
|--------------|---------------|-----------------------------|---------------------------------------|---------------------------------------|------------------------------|-----------------|
| | Models | Normal (n = 330) | High FPG/FPI (n = 235) | Pre- Diabetes (n = 92) | Diabetes (n = 68) | p-value* |
| LVM | Age-adjusted | 125 | 127 | 136 | 136 | <0.0001 |
| | MV-adjusted | 129 | 125 | 129 | 131 | 0.16 |
| LVEDV | Age-adjusted | 146 | 144 | 140 | 151 | 0.11 |
| | MV-adjusted | 149 | 143 | 136 | 148 | 0.001 |
| Women | | | | | | |
| | Models | Normal (n = 533) | High FPG/FPI (n = 207) | Pre- Diabetes (n = 84) | Diabetes (n = 54) | p-value* |
| LVM | Age-adjusted | 83 | 88 | 95 | 93 | <0.0001 |
| | MV-adjusted | 86 | 85 | 86 | 86 | 0.96 |
| LVEDV | Age-adjusted | 106 | 111 | 114 | 113 | 0.0002 |
| | MV-adjusted | 109 | 109 | 107 | 107 | 0.75 |

Cells present adjusted mean values of cardiac measures; *p-value for trend.

MV-adjusted = multivariable-adjusted; LVM = left ventricular mass; LVEDV = left ventricular end-diastolic volume. “Normal” group includes participants with both fasting plasma glucose \leq 100mg/dl and fasting plasma insulin \leq 75th percentile of distribution; “High FPG/FPI” group includes those with either fasting plasma insulin $>$ 75th percentile of distribution or fasting plasma glucose $>$ 100mg/dl (but not both); and “pre-diabetes” includes those without diabetes but with both fasting plasma glucose $>$ 100mg/dl and fasting plasma insulin $>$ 75th percentile of distribution.

MV model adjusted for age, body mass index, systolic blood pressure, cardioactive drug therapy and smoking status.