Association Between Elevated Fasting Glucose, in the Absence of Diabetes, and Increased Left Ventricular Mass in Women

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INTRODUCTION: Increased left ventricular (LV) mass is an independent risk factor for excess morbidity and mortality. Diabetes mellitus has been associated with alterations in cardiac structure and function, which may be sex-specific, and in the United States, over 20 million adults have diabetes. Further, over 50 million adults have elevated fasting glucose (EFG) and are at risk for diabetes. Hyperglycemia appears to be a continuous risk factor for cardiovascular disease, but the relationship between elevated fasting glucose levels in the absence of actual diabetes and LV mass and function determined by cardiovascular magnetic resonance (CMR) is not well characterized.

METHODS:

Subjects: Adults from the Framingham Heart Study Offspring cohort, who have undergone comprehensive ("Cycle") examinations every 3-5 years since 1974, were recruited for CMR. To be included in this report, subjects were known to be free of clinical cardiovascular disease (history of stable angina, myocardial infarction, positive stress test or significant stenosis by catheterization, stroke or transient ischemic attack, intermittent claudication or heart failure). Subjects were also free of hypertension (SBP≤140 mmHg and DBP≤90 mmHg on all Cycle examinations and never on antihypertensive medications), without history of diabetes, in sinus rhythm and without contraindications to CMR. Of all subjects scanned, 799 met entry criteria and were stratified by fasting glucose levels: normal (NL) with fasting glucose ≤100 mg/dL and EFG with fasting glucose from 101-125 mg/dL.

CMR Acquisition and Analysis: Imaging was performed on a 1.5T system (Philips) using a 5-element cardiac array coil for RF signal reception. Following scout imaging, a 2D breath hold ECG-gated SSFP sequence was used to encompass the ventricles in the LV short-axis orientation. Imaging parameters included 1.56x1.92-mm^2 in-plane spatial resolution and 10-mm slice thickness without interslice gap; temporal resolution was 30-40 ms. LV epicardial and endocardial contours were manually segmented by a single expert observer blinded to subject identity and characteristics. A summation of disks method was used to determine LV volumes and mass. Ejection fraction (EF) was the ratio of stroke volume to end-diastolic cavity volume (EDV). LV geometry (or concentricity) was assessed by "relative myocardial volume" (RMV), the ratio of LV myocardial volume to EDV. RMV was used instead of LV mass/EDV as RMV is a dimensionless ratio.

Statistics: Continuous variables are summarized as mean±SD. Subjects were stratified by sex and FG levels. LV mass was indexed to height (HT, m), body surface area (BSA, m^2) and to fat-free mass (FFM, kg). FFM was calculated using the formula of Kvist et al [1], validated against volumetric assessment of whole body adiposity by computed tomography. Group comparisons, adjusted for age, were made using 2-sample t test with $p<0.05$ considered significant.

RESULTS: 300 subjects (134 women, 166 men) had EFG. Those with EFG were significantly older than NL subjects (women: 63±8 years vs. 61±8, men 62±8 vs. 60±8, $p<0.05$ both). Among women (Table), EFG subjects had greater LV mass than NL subjects, and these differences persisted after indexation of mass to HT. After indexation to BSA, EFG subjects still had greater LV mass than NL, but this difference was no longer significant (p=NS). Indexation to FFM revealed significantly greater LV mass in women with EFG. Among men, there were no differences in LV mass between NL and EFG subjects regardless of method of indexation. There were no differences in LV geometry between NL and EFG subjects for either men or women. EF was significantly ($p<0.05$) greater in women (NL: 67.8±5.4, EFG 67.9±5.2) than men (NL: 65.1±5.8, EFG: 65.3±5.6), but there were no differences between NL and EFG subjects within each sex.

CONCLUSIONS: Elevated fasting glucose is associated with increased LV mass in women but not men. Among women, LV mass was not different between NL and EFG subjects after indexation to BSA, but remained significant after indexation to FFM, suggesting that differences in LV mass are associated with adiposity, as reflected by body surface area. Despite the greater LV mass in EFG subjects, there was no difference in LV concentricity as compared with NL subjects. This may suggest that EFG, in the absence of history of hypertension, is associated with an eccentric hypertrophy in women (though there is currently no standard definition of concentricity/eccentricity using volumetric measures of LV mass/myocardial volume and cavity volume). There were no differences in overall systolic function between NL and EFG subjects, though as previously noted [2,3], women had greater EF than men.

WOMEN	Normal (n=357)	EFG (n=134)	p-value
LV mass, g	80.4±13.9	84.7±16.4	<0.001
LV mass/HT, g/m	49.5±7.9	52.1±9.6	<0.001
LV mass/BSA, g/m^2	46.7±6.6	47.2±7.0	NS
LV Mass /FFM, g/kg	1.96±0.29	2.03 ±0.34	0.012
RMV	0.76±0.11	0.78±0.11	NS

References: [1] H Kvist, et al. Am J Clin Nutr 1988;48:1351-61. [2] AK Chung, et al, Circulation 2006; 113: 1597. [3] CJ Salton, et al, Circulation 2006; 114: 669 Suppl. S