Relationship of Cardiorespiratory Fitness and Adiposity With Left Ventricular Strain in Middle-Age Adults (from the Dallas Heart Study)

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Low cardiorespiratory fitness (CRF) and obesity are significant risk factors for heart failure (HF). However, given the inverse association between CRF and obesity, the independent contributions of low CRF and adiposity toward HF risk are not well established. We evaluated the association of CRF and measures of adiposity with left ventricular (LV) peak systolic strain—a subclinical measure of LV dysfunction—among the Dallas Heart Study phase II participants without cardiovascular disease who had CRF estimated using a submaximal treadmill test and LV systolic circumferential strain assessment by tissue-tagged cardiac magnetic resonance imaging. Peak midwall systolic circumferential strain (Ecc) was determined by harmonic phase imaging. Associations of CRF and adiposity measures with Ecc were determined using adjusted linear regression analysis. A total of 1,617 participants were included in the analysis. After adjustment for baseline risk factors, higher waist circumference (WC) and lower CRF were associated with higher Ecc (WC: $\beta = 0.07$; $p = 0.01$; CRF: $\beta = -0.17$; $p = < 0.0001$), whereas % body fat and body mass index were not associated with Ecc. The relationship between WC and Ecc was attenuated completely after additional adjustment for CRF. In contrast, the association between CRF and Ecc did not attenuate after additional adjustment for WC and other measures of LV structure and function ($\beta = -0.18$; $p = < 0.0001$). Taken together, our study findings suggest that lower CRF, but not measures of adiposity, is associated with greater impairment in LV strain independent of LV mass and ejection fraction. **(Am J Cardiol 2017;120:1405–1409)**

There is an inverse association between levels of cardiorespiratory fitness (CRF) and adiposity.[1] Both low levels of CRF and increased adiposity are associated with increased risk of adverse cardiovascular (CV) events, including heart failure (HF).[2–4] However, the mechanism through which low CRF and adiposity might independently predispose to an increased risk of HF is not well understood. Furthermore, the extent to which low CRF and/or adiposity independently influence CV risk remains incompletely understood.

Subclinical left ventricular (LV) systolic dysfunction is an independent predictor of HF risk.[5–8] However, LV ejection fraction (EF), the most commonly used parameter to assess systolic function, may miss subtle abnormalities in myocardial contractility in otherwise healthy individuals. In contrast, abnormalities in LV peak systolic strain, a measure of myocardial shortening, is a sensitive marker of subclinical myocardial dysfunction that has been associated with greater risk of HF.[9,10] Understanding the contributions of low CRF and/or adiposity on abnormalities in LV strain is an important step to characterizing the progression from asymptomatic low-fit and obese stage to clinical HF. Accordingly, we examined the independent associations between CRF, measures of adiposity, and LV strain among healthy middle-age adults. We hypothesized that low CRF and higher levels of adiposity would be associated with greater impairment in LV strain.

Methods

The Dallas Heart Study (DHS) is a longitudinal, multiethnic probability-based cohort study of Dallas County residents with deliberate oversampling of black participants to ensure a 1-to-1 ratio of black and nonblack participants. Recruitment

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procedures and study design have been reported previously.[11] Enrollment of the original group of participants occurred in 2000 to 2002. Study participants, along with their spouses, were invited for a repeat examination in 2007 to 2009 for DHS phase 2. Each participant underwent a health examination that included blood pressure measurements, anthropometry, blood and urine sampling, imaging studies, and CRF assessment. All participants provided written informed consent. The institutional review board of the University of Texas Southwestern Medical Center approved the study. Of the 3,403 subjects who participated in the DHS phase 2, complete cardiac magnetic resonance imaging (MRI) examination was performed in 2,106 participants. Of those, 2,037 had tagged MRI strain data available of sufficient quality for strain analysis. For the present study, we excluded participants with CV disease (n = 55), depressed EF (<45%, n = 22), baseline use of β blockers (n = 162), and missing CRF data (n = 181; 140 with no exercise treadmill test and 41 excluded because of exercise heart rate greater than 100% or less than 50% of maximal predicated heart rate at the target workload). Participants on β blockers were excluded as it may have confounded the CRF level assessment by lowering the submaximal exercise heart rate. The final study population included 1,617 participants. The details regarding assessment of baseline demographic, anthropometric, and clinical characteristics have been published previously.[11] Measures of adiposity included in our study as exposure variables of interest were body mass index (BMI), waist circumference (WC), and DEXA-derived percent body fat. CRF was evaluated in DHS phase 2 by using a submaximal exercise treadmill test as previously described.[12] Study participants underwent a cardiac MRI using a 3-T MRI system (Philips Medical Systems, Best, the Netherlands). LV mass and volume measurements were obtained from short-axis breath-hold ECG-gated cine CMR and MASS software (Medis Medical Imaging Systems, Leiden, the Netherlands) using methods as previously reported.[13] Stroke volume was calculated as the difference between end-diastolic and end-systolic LV volumes. CMR tissue tagging of the myocardium was performed in the horizontal and vertical planes of LV short-axis slices at the midventricular level. Circumferential strain analysis was performed offline using commercially available harmonic phase imaging software (HARP, Diagnosoft Virtue 5.04; Diagnosoft, Palo Alto, California) to determine peak systolic strain in 6 midwall segments from the midventricular short-axis slice.[14,15] The strain values measured for different segments at different time points of the cardiac cycle were used to generate a global circumferential strain curve, with peak systolic circumferential strain being the most negative point on the curve.[15] Peak systolic circumferential strain, which represents LV shortening in the circumferential plane, normally has a negative value, and less negative values indicate decreased shortening and thus greater impairment in myocardial contractility.

The demographic and clinical characteristics of the study participants were compared across age- and gender-adjusted quartiles of CRF using the chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. The proportion of participants with impaired peak systolic circumferential strain, defined based on data-derived cutoff of >80th percentile, was compared across age- and gender-adjusted CRF, BMI, and WC quartiles. Separate multivariable adjusted linear regression analyses models were constructed to determine the independent association between CRF, adiposity measures, and peak systolic circumferential strain. Model 1 was adjusted for CV risk factors (age, sex, ethnicity, smoking status, systolic blood pressure, hypertension status, blood glucose, and diabetes status) and adiposity measures (BMI, WC, and percent body fat in separate models); Model 2 was additionally adjusted for CRF levels; and Model 3 was further adjusted for LV mass and LV EF. We also tested for statistical interaction between CRF and race/ethnicity, CRF and gender for the outcome of LV strain. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Inc., Cary, North Carolina).

Results

Baseline characteristics of the study participants are compared across age- and gender-adjusted quartiles of CRF in Table 1. Compared with the low-fit participants (Quartile 1), high-fit participants (Quartile 4) were more commonly white, had lower burden of CV risk factors such as hypertension, diabetes, and dyslipidemia, had lower measures of adiposity including BMI, WC, and percent body fat, had higher measures of LV dimension, higher stroke volume, and more negative peak systolic circumferential strain indicating better LV contractility.

Figure 1 compares the prevalence of peak systolic circumferential strain impairment across age- and gender-adjusted quartiles of CRF, BMI, and WC. The proportion of participants with impaired strain decreased significantly with higher CRF levels (29% in CRF Quartile 1 vs 18% in CRF Quartile 4, P-trend <0.0001). In contrast, higher BMI and WC were associated with a greater prevalence of peak systolic circumferential strain impairment (21% in BMI Quartile 1 vs 27% in BMI Quartile 4, P-trend = 0.04; 20% in WC Quartile 1 vs 28% in WC Quartile 4, P-trend =0.0005).

After adjustment for demographic characteristics and baseline cardiovascular risk factor burden, higher WC and lower CRF were also associated with higher peak systolic circumferential strain (WC: $\beta = 0.07$, $p = 0.01$; CRF: $= -0.17$, $p = < 0.0001$), whereas percent body fat and BMI were not associated with peak systolic circumferential strain after multivariable adjustment (percent body fat: $\beta = 0.07$, $p = 0.09$; BMI: $\beta = 0.04$, $p = 0.17$). The relation between WC and LV strain was attenuated and no longer significant after additional adjustment for CRF ($\beta = 0.02$, $p = 0.22$; Table 2). In contrast, the association between CRF and peak systolic circumferential strain did not attenuate after additional adjustment for WC and other measures of LV structure (LV mass) and function (EF) ($\beta = -0.18$, $p = < 0.0001$; Table 2). Among other participant characteristics, male gender, higher LV mass, and lower EF were each associated with greater peak systolic circumferential strain impairment in the most adjusted model. No significant interaction was observed between gender, ethnicity/race, and CRF for the outcome of peak systolic circumferential strain.

Discussion

The principal finding observed in the present study is that low CRF is independently associated with subclinical