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CLINICAL RESEARCH

Association of Cardiorespiratory Fitness With Left Ventricular Remodeling and Diastolic Function

The Cooper Center Longitudinal Study

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Objectives This study sought to compare the cross-sectional associations between fitness and echocardiographic measures of cardiac structure and function.

Background Cardiorespiratory fitness is inversely associated with heart failure risk. However, the mechanism through which fitness lowers heart failure risk is not fully understood.

Methods We included 1,678 men and 1,247 women from the Cooper Center Longitudinal Study who received an echocardiogram from 1999 to 2011. Fitness was estimated by Balke protocol (in metabolic equivalents) and also categorized into age-specific quartiles, with quartile 1 representing low fitness. Cross-sectional associations between fitness (in metabolic equivalents) and relative wall thickness, left ventricular end-diastolic diameter indexed to body surface area, left atrial volume indexed to body surface area, left ventricular systolic function, and E/e′ ratio were determined using multivariable linear regression analysis.

Results Higher levels of mid-life fitness (metabolic equivalents) were associated with larger indexed left atrial volume (men: beta = 0.769, $p < 0.0001$; women: beta = 0.879, p value $\leq$0.0001) and indexed left ventricular end-diastolic diameter (men: beta = 0.231, $p < 0.001$; women: beta = 0.264, $p < 0.0001$). Similarly, a higher level of fitness was associated with a smaller relative wall thickness (men: beta = –0.002, p = 0.04; women: beta = –0.005, $p < 0.0001$) and E/e′ ratio (men: beta = –0.11, p = 0.003; women: beta = –0.13, p = 0.01). However, there was no association between low fitness and left ventricular systolic function (p = NS).

Conclusions Low fitness is associated with a higher prevalence of concentric remodeling and diastolic dysfunction, suggesting that exercise may lower heart failure risk through its effect on favorable cardiac remodeling and improved diastolic function. (J Am Coll Cardiol HF 2014;2:238–46)

Higher levels of self-reported physical activity and measured fitness are associated with a lower risk for heart failure that is independent of established heart failure risk factors such as obesity, diabetes, and hypertension (1–4). Whereas the potential mechanisms through which exercise might lower heart failure risk are not completely understood, multiple lines of evidence suggest that higher levels of exercise might have a direct effect on cardiac structure and function. In particular, individuals who report high levels of exercise across the lifespan have more compliant left ventricles than sedentary, age-matched control subjects do (5,6). These findings suggest the hypothesis that higher levels of exercise may lower the risk for heart failure with preserved ejection fraction (HFpEF). Given the failure of numerous therapies for the treatment and prevention of HFpEF, this would

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represent an important observation that could have significant public health implications (7).

The associations between intense physical activity and fitness and physiologic cardiac remodeling and improved early diastolic filling are well established in elite athletes (8–10), but the effects of exercise on cardiac structure and function within the continuum of normal fitness levels are not known. Echocardiography represents a valuable potential intermediate phenotype that can provide important insights into cardiac structure and both systolic and diastolic function. The presence of pathologic ventricular remodeling patterns (11–13) have been identified as important intermediates in the pathway to heart failure. Ventricular remodeling is associated with increased volume and altered chamber geometry that develops in response to a myocardial injury and increased wall stress. Three patterns of left ventricular (LV) remodeling have been identified on the basis of the measures of LV mass index and relative wall thickness (RWT): concentric remodeling (normal LV mass index and increased RWT); eccentric hypertrophy (increased LV mass index and normal RWT); and concentric hypertrophy (increased LV mass index and increased RWT) (14). Similarly, subclinical systolic and diastolic dysfunction has been shown to be an important determinant of adverse cardiovascular outcomes (15–18). Specifically, subclinical systolic dysfunction carries increased risk of heart failure with reduced ejection fraction and asymptomatic diastolic dysfunction increases the risk of future HFpEF (15–18).

The purpose of this study was to characterize the association between measured cardiorespiratory fitness and cardiac structure and function in the Cooper Center Longitudinal Study. We hypothesized that higher fitness levels would be associated with a lower prevalence of diastolic dysfunction and a lower prevalence of concentric remodeling/hypertrophy. We further hypothesized that there would be no association between fitness and systolic function.

Methods

Study participants. The CCLS (Cooper Center Longitudinal Study) is an ongoing study derived from patients at the Cooper Clinic, a preventive health clinic in Dallas, Texas, and has previously been well described (19,20). All participants are either self-referred to the clinic or are referred by their employer or personal physician. They are predominantly Caucasian and from the middle to upper socioeconomic strata. For the present study, we included patients from the CCLS who received both a clinically indicated echocardiogram at the clinic between 1999 and 2011 and a standardized medical examination by a physician including a maximal treadmill exercise test. Echocardiograms were performed for a broad range of indications (Online Table). This study was approved by both the Cooper Institute and the University of Texas Southwestern Institutional Review Boards.

After excluding 14 participants with severe valvular disorders, we included 1,678 men and 1,247 women in the final study sample who received an echocardiogram within 3 months of their examination and measured fitness at the clinic. There was a low prevalence of low ejection fraction (EF) and abnormal stress echo in the study cohort, and those subjects were included in the final analysis. Finally, because tissue Doppler was incorporated into the standard echocardiographic examination at the Cooper Clinic in 2003, 42% of the participants were missing tissue Doppler data. Therefore, we included 1,235 participants for the tissue Doppler analyses.

Abbreviations and Acronyms

BSA = body surface area

BMI = body mass index

EF = ejection fraction

HFpEF = heart failure with preserved ejection fraction

LA Vol = left atrial volume

LA Vol/BSA = left atrial volume indexed to body surface area

LV = left ventricular

LVEDD = left ventricular end-diastolic diameter

LVEF = left ventricular ejection fraction

LVMI = left ventricular mass index

PWT = posterior wall thickness

Q = quartile

RWT = relative wall thickness

SWT = septal wall thickness

Data collection. Details of the clinical examination for CCLS participants have been reported previously (19,20). Medical history of diabetes, hypertension, coronary artery disease, smoking history, fasting blood glucose, blood pressure, and body mass index (BMI) (calculated from weight and height) were collected during the physical examination. Medications were extracted from the medical record. Hypertension was defined as either a systolic blood pressure >140 mm Hg, self-reported hypertension, or use of antihypertensive drug. Diabetes was defined as the presence of a fasting blood sugar ≥126 mg/dl, self-reported diabetes, or use of antihyperglycemic drug.

Echocardiographic data. All echocardiograms were performed using a GE Vivid 7 (Milwaukee, Wisconsin) and were read by a staff cardiologist at the clinic at the time the echocardiogram was done. The following variables were gathered from the resting echocardiograms, including the indication for the echocardiogram, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter, posterior wall thickness (PWT), septal wall thickness (SWT), left atrial diameter, left ventricular ejection fraction (LVEF), valvular stenosis/regurgitation, mitral inflow Doppler (E-wave, A-wave, and deceleration time), and tissue Doppler (e′) of the lateral mitral annulus.

The following echocardiographic variables were defined in accordance with standard definitions: LVEF: (LV end-diastolic volume − LV end-systolic volume) ÷ LV end-diastolic volume, where both the LV end-diastolic volume and LV end-systolic volume were estimated using the modified Simpson rule (biplane method of disks): LV mass (indexed to body surface area) $[0.8 \times \{1.04\ (\text{LVEDD} + \text{PWT} + \text{SWT})^3 - (\text{LVEDD})^3\} + 0.6\ \text{g}]$; RWT ($2 \times$ PWT/LVEDD). Left atrial volume (LA Vol)