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Left Ventricular Diastolic Function and Exercise Capacity in Community-Dwelling Adults $\geq$ 65 Years of Age without Heart Failure

Gilbert J. Perry, MD^{1,2}, Mustafa I. Ahmed, MD², Ravi V. Desai, MD³, Marjan Mujib, MBBS, MPH², Michael Zile, MD⁴, Xuemei Sui, MD, MPH⁵, Inmaculada B. Aban, PhD², Yan Zhang, MS, MSPH², Jose Tallaj, MD^{1,2}, Richard M. Allman, MD^{2,1}, Wilbert S. Aronow, MD⁶, Jerome L. Fleg, MD⁷, and Ali Ahmed, MD, MPH^{2,1}

¹Veterans Affairs Medical Center, Birmingham, AL

²University of Alabama at Birmingham, Birmingham, AL

³Lehigh Valley Hospital, Allentown, PA

⁴Medical University of South Carolina, Charleston, SC

⁵University of South Carolina, Columbia, SC

⁶New York Medical College, Valhalla, NY

⁷National Heart, Lung, and Blood Institute, Bethesda, MD

Abstract

Left ventricular diastolic dysfunction (LVDD) has been reported to have strong correlation with exercise capacity. However, this relationship has not been studied extensively in community-dwelling older adults. Data on pulse and tissue Doppler echocardiographic estimates of resting early (E) and atrial (A) transmitral peak inflow and early (Em) mitral annular velocities, and six-minute walk test were obtained from 89 community-dwelling older adults (mean age, 74; range, 65–93 years; 54% women), without a history of heart failure. Overall, 47% had cardiovascular morbidity and 60% had normal diastolic function (E/A 0.75–1.5 and $E/Em < 10$). Among the 36 individuals with LVDD, 83%, 14% and 3% had grade I ($E/A < 0.75$, regardless of E/Em), II (E/A 0.75–1.5 and $E/Em \geq 10$) and III ($E/A > 1.5$ and $E/Em \geq 10$) LVDD respectively. Those with LVDD were older (77 versus 73 years; $p=0.001$) and tended to have a higher prevalence of cardiovascular morbidity (58% versus 40%; $p=0.083$). LVDD negatively correlated with six-minute walk distance (1013 versus 1128 feet; $R=-0.25$; $p=0.017$). This association remained significant despite adjustment for cardiovascular morbidity ($R=-0.35$; $p=0.048$), but lost significance when adjusted for age ($R=-0.32$; $p=0.105$), both age and cardiovascular morbidity ($R=-0.38$; $p=0.161$), and additional adjustment for sex, race, body mass index, and systolic blood pressure ($R=-0.44$; $p=0.365$). In conclusion, most community-dwelling older adults without heart failure had normal left ventricular diastolic function or grade-I LVDD. Although LVDD was associated with decreased performance on a six-minute walk test, that association was no longer evident after adjustment for age, body mass index and cardiovascular morbidity.

Corresponding author: Ali Ahmed, MD, MPH, University of Alabama at Birmingham, 1530 3rd Ave South, CH-19, Ste-219, Birmingham AL 35294-2041; **Tel.:** 1-205-934-9632; **Fax:** 1-205-975-7099; aahmed@uab.edu.

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Keywords

Left Ventricular Diastolic Function; Exercise Capacity; Older Adults; Cardiovascular Morbidity

Left ventricular (LV) diastolic function is an independent predictor of exercise capacity in heart failure (HF).¹ LV diastolic function has also been shown to be associated with functional capacity in younger adults referred for exercise testing.^{2, 3} Aging is strongly associated with a decline in both LV diastolic function and functional capacity.³⁻¹⁰ However, the relationship between LV diastolic function and functional capacity has not been extensively studied in relatively healthy, community-dwelling older adults. Further, the extent to which the age-associated decline in LV diastolic function contributes to the decline in functional capacity among community-dwelling older adults remains uncertain. The purpose of the current study was to examine the association between age, LV diastolic function and physical function in a cohort of community-dwelling ambulatory older volunteers without heart failure (HF).

Methods

Community-dwelling ambulatory older adults, ≥ 65 years, without a history of HF, valvular heart disease or atrial fibrillation, were eligible for participation. Participants were recruited by community advertisements between 2003 and 2006. After obtaining informed consent, participants were interviewed by trained research assistants and then underwent electrocardiography, echocardiography and a 6-minute walk test. Participants with electrocardiographic or echocardiographic evidence of atrial fibrillation, LV ejection fraction $< 45\%$, and those with severe aortic or mitral insufficiency were excluded. Local institutional review boards approved the study protocol.

All echocardiographic measurements were performed by trained technicians under direct supervision of a trained echocardiographer (G.J.P.) using Philips ATL 5000 HDI ultrasound (Bothell, Washington) equipment. The technician and echocardiographer were blinded to participants' cardiovascular morbidities. LV mass (indexed to height and weight) and LV ejection fraction were measured according to the recommendations of the American Society of Echocardiography.¹¹ Early (E) and atrial (A) transmitral maximal inflow velocities at the tips of the mitral valve leaflets by pulse Doppler, and early (Em) and atrial (Am) mitral annular velocity by pulse tissue Doppler at the base of the lateral wall 5-10 mm below the mitral annulus area in the apical 4-chamber view, were obtained using standard techniques.¹² Participants were stratified into grade 0 (normal), I, II, or III LV diastolic dysfunction (LVDD) as follows: grade 0 or normal diastolic function (E/A 0.75–1.5 and E:Em < 10), grade I (E/A < 0.75 regardless of E:Em), grade II (E/A 0.75–1.5 and E:Em ≥ 10), and grade III (E/A > 1.5 and E:Em ≥ 10).¹³

The 6-minute walk test, a validated and reliable measure of functional exercise capacity,¹⁴⁻¹⁶ was performed indoors, along a flat, firm surface, by a trained technician, following a written protocol developed according to recommendations made by the American Thoracic Society guideline.¹⁵ Briefly, participants were instructed to walk back and forth for 6 minutes. They could slow down or stop and rest as necessary and then resume walking when they could. They were also gently encouraged to walk as fast as possible throughout the test as required. At the end of the walk, they were asked if they felt any symptoms such as pain, shortness of breath or fatigue. Participants were categorized to have low 6-minute walk test distance if they had walked < 1059 feet (median) in 6 minutes.

We categorized participants into two groups based on the presence of LVDD. We compared baseline patient characteristics of participants, including findings from the echocardiographic and 6-minute walk test, by the presence or absence of LVDD using chi-square and Student t-tests as appropriate. Linear regression models were used to determine relationships between LVDD and 6-minute walk test, adjusting for age alone, cardiovascular morbidities alone, both and additional adjustment for sex, race, body mass index and systolic blood pressure. All tests were two-tailed, and a p-value of <0.05 was considered statistically significant. All statistical analyses were conducted using the SPSS 15 (SPSS Inc., Chicago, IL).

Results

Participants (n=89) had a mean ($\pm$ SD) age of 74 ($\pm$ 6) years, 54% were women, 16% were non-white, and 47% had at least one cardiovascular morbidity. Overall, 53 (60%) participants had normal LV diastolic function, and 36 participants had LVDD. Of those with LVDD, 83% (30/36) had grade I, 14% (5/36) had grade II and 3% (1/36) had grade III LVDD. Except for older age and a higher prevalence of diabetes among those with LVDD, most other baseline characteristics including baseline history of physical function were balanced between the groups (**Table 1**). Participants had a mean ($\pm$ SD) LV ejection fraction of 57% ($\pm$ 3%), mean E/A ratio of 0.86 ($\pm$ 0.23), peak Em wave of 10 ($\pm$ 2) cm/sec, and E/Em ratio of 7.0 ($\pm$ 2.3; **Table 2**). As expected, the E/A ratio and peak Em were lower in those with LVDD. However, E/Em ratio was similar between the groups.

Associations of age with parameters of LV diastolic function are displayed in **Figure 1**. Resting Em was negatively associated with age ($R=-0.41$; $p<0.001$), regardless of cardiovascular morbidities (**Figure 1**). However, the overall significant association between age and E/A ratio ($R=-0.24$ $p=0.026$) was only significant in those without cardiovascular morbidity ($R=0.44$; $p=0.002$) but not in those with cardiovascular morbidity ($R=0.04$, $p=0.803$; **Figure 1**). Resting E/Em was positively associated with increased age in the overall population ($R=0.29$, $p=0.007$), and in those with cardiovascular morbidity ($R=0.32$; $p=0.038$), but not in those without ($R=0.13$; $p=0.371$; **Figure 1**).

Overall, participants had a mean 6-minute walk test distance of 1081 ($\pm$ 226) feet, which was lower for those with LVDD (1012 versus 1128 feet, $P=0.017$; **Table 2**). Few participants reported symptoms during their walks, the prevalence of which was not significantly different between the two groups. LVDD was associated with shorter 6-minute walk test distance (1012 versus 1128 feet for those without LVDD; $p=0.017$; **Table 2**). The association between LVDD and 6-minute walk test distance ($R=-0.25$, $p=0.017$) remained significant despite adjustment for cardiovascular morbidity ($R=-0.35$; $p=0.048$), but lost significance when adjusted for age ($R=-0.32$; $p=0.105$), both age and cardiovascular morbidity ($R=-0.38$; $p=0.161$), and after additional adjustment for sex, race, body mass index, and systolic blood pressure ($R=-0.44$; $p=0.365$; **Table 3**). Neither Em nor E/Em was significantly associated with 6-minute walk test distance ($R=0.04$, $p=0.739$ and $R=0.05$, $p=0.676$; **Figure 2**). However, age was negatively associated with 6-minute walk test distance ($R=0.25$; $p=0.020$; **Figure 3**).

Discussion

Findings from the current study demonstrate that most community-dwelling older adults without HF had preserved LV diastolic function, and that those with LVDD had rather mild LVDD. We also observed that the presence of LVDD was associated with decreased performance in a 6-minute walk test. However, when adjusted for age, this association lost significance, suggesting that older age of those with LVDD explains most of the LVDD-

associated decline in 6-minute walk test distance. The persistence of a non-significant association after multivariable adjustment for other risk factors suggested lack of an independent association between LVDD and 6-minute walk test performance in healthy older adults.

Resting echocardiographic assessment of diastolic function commonly assesses two diastolic properties, early relaxation, and LV filling pressure. Most of those with LVDD in our study had mild LVDD (grade I), which is characterized by diminished early relaxation in the absence of elevated LV filling pressure. Early relaxation has traditionally been assessed by the E/A ratio, and more recently, by the recoil velocity of the mitral annulus, Em, which has been shown to correlate well with the time constant of isovolumic pressure decay, tau.¹⁷ Advanced stages of LVDD, often associated with an elevated resting LV filling pressure, have been shown to be important predictors of exercise intolerance in multiple cross-sectional studies.^{2, 3, 13, 18} However, in the population of asymptomatic and relatively healthy community-dwelling older adults, the prevalence of advanced LVDD was very low, which likely explains the lack of a significant independent association with physical function.

Grewal et al reported an association between grade I LVDD and diminished exercise capacity in a large middle-aged population (mean age, 58 years) referred for exercise echocardiography for clinical indications.³ Diminished E/A ratio or Em is pathologic in middle-aged populations, indicating LVDD, and is highly associated with underlying cardiovascular morbidity such as diabetes, coronary artery disease, hypertension, and adverse outcomes.¹³ The presence of even mild LVDD in middle-aged subjects thus identifies a subset of the population with a high prevalence of cardiovascular morbidity, such that an association with diminished exercise capacity is not unexpected. Conversely, a decline in early relaxation by Em or E/A ratio is normal with aging, often not prevented by training, and has been demonstrated even in master athletes.¹⁹⁻²⁵ However, we observed that among the relatively healthy community-dwelling older adult cohort in our study, most had normal LV diastolic function, and among those with LVDD, very few had advanced LVDD.

Some limitations of the current study should be acknowledged. Diastolic function was measured at rest; hence, it is possible some of the functional decline may have been due to LVDD that manifests only during exercise. We used the 6-minute walk test, which is a measure of submaximal rather than maximal exercise capacity. However, the 6-minute walk test has been shown to correlate both with symptom-limited exercise time and peak VO₂ in older adults.^{15, 26} Additionally, the 6-minute walk test may be a more realistic measure of physical function in older adults, most of whom are unlikely to participate in activities of maximal physical capacity. In conclusion, LVDD is relatively uncommon and mild in community-dwelling older adults without heart failure, and lacks an independent association with six-minute walk test performance.

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Figure 1. Scatter plots showing correlations of parameters of left ventricular diastolic function with age.

Figure 2.
Scatter plots showing correlations of parameters of left ventricular diastolic function with 6-minute walk test distance, stratified for those with (closed circle) and without (open circles) cardiovascular morbidity

Figure 3.
Scatter plot showing correlation age with 6-minute walk test distance, stratified for those with (closed circle) and without (open circles) cardiovascular morbidity

Table 1

Baseline characteristics by left ventricular diastolic dysfunction (LVDD) *

N (%) or mean ($\pm$ SD)	All (n=89)	LVDD		P Value
		No (n=53)	Yes (n=36)	
Age (years)	74 ($\pm$ 6)	73 ($\pm$ 5)	77 ($\pm$ 6)	0.001
Women	48 (54%)	26 (62%)	22 (45%)	0.263
Non-white	14 (16%)	7 (13%)	7 (19%)	0.428
Married	41 (46%)	27 (51%)	14 (39%)	0.263
Education college or higher	69 (78%)	43 (81%)	26 (72%)	0.323
Income $\geq$ 25k	47 (53%)	26 (49%)	21 (51%)	0.390
Smoker				
Current	2 (2%)	1 (2%)	1 (3%)	0.574
Past	29 (33%)	15 (29%)	14 (39%)	
Self-reported general health good or fair	51 (57%)	27 (51%)	24 (67%)	0.141
Physical function / symptoms				
Dyspnea on exertion in the past 12 months	13 (15%)	8 (15%)	5 (14%)	0.846
Able to climb up one flight of stairs	86 (97%)	51 (96%)	35 (97%)	0.798
Climb more than two flights of stairs daily	39 (44%)	19 (36%)	20 (56%)	0.066
Able to walk about three city blocks	87 (98%)	51 (96%)	36 (100%)	0.238
Walked about three city blocks last week	13 (15%)	8 (15%)	5 (14%)	0.874
Less active than someone similar age	59 (66%)	34 (64%)	25 (69%)	0.604
Body mass index (kg/m ²)	25 ($\pm$ 4.6)	25 ($\pm$ 4.6)	26 ($\pm$ 4.7)	0.294
Pulse (beats per minute)	64 ($\pm$ 10.0)	64 ($\pm$ 10)	65 ($\pm$ 10)	0.489
Systolic blood pressure (mm Hg)	136 ($\pm$ 18.8)	134 ($\pm$ 17)	139 ($\pm$ 21)	0.197
Diastolic blood pressure (mm Hg)	70 ($\pm$ 10.4)	68 ($\pm$ 10)	72 ($\pm$ 11)	0.163
Cardiovascular morbidities	42 (47%)	21 (40%)	21 (58%)	0.083
Hypertension	33 (37%)	16 (30%)	17 (47%)	0.103
Coronary artery disease	7 (8%)	4 (8%)	3 (8%)	0.892
Diabetes mellitus	6 (6.7%)	1 (2%)	5 (14%)	0.027
Stroke or transient ischemic attack	4 (4.5%)	2 (4%)	2 (6%)	0.705
Peripheral vascular disease	3 (3%)	2 (4%)	1 (3%)	0.786
Medications				
Angiotensin-converting enzyme inhibitor or Angiotensin II receptor blocker	9 (10%)	6 (11%)	3 (8%)	0.646
Beta blocker	12 (13%)	10 (19%)	2 (6%)	0.071
Diuretic	8 (9%)	5 (9%)	3 (8%)	0.859
Electrocardiogram				
Left ventricular hypertrophy	2 (2%)	1 (2%)	1 (3%)	0.781
First degree heart block	8 (10%)	2 (4%)	6 (18%)	0.035

* Participants were stratified into normal LV diastolic function (grade 0; E/A 0.75–1.5 and E:Em <10) and LVDD. Those with LVDD were further classified as follows: grade I (E/A <0.75 regardless of E:Em), grade II (E/A 0.75–1.5 and E:Em $\geq$ 10), and grade III (E/A >1.5 and E:Em $\geq$ 10)

Table 2

Baseline echocardiographic characteristics and six-minute walk test results by left ventricular diastolic dysfunction (LVDD)

N (%) or mean (±SD)	All (n=89)	LVDD		P Value
		No (n=53)	Yes (n=36)	
Echocardiogram				
Ejection fraction (%)	57 (±3)	57 (±3)	56 (±3)	0.703
E to A ratio	0.86 (±0.23)	0.96 (±0.18)	0.71 (±0.21)	<0.001
Peak E wave (cm/sec)	65 (±16)	61 (±12)	68 (±19)	0.033
Peak A wave (cm/sec)	78 (±17)	72 (±14)	86 (±17)	<0.001
Peak Em wave (m/sec)	9.8 (±2.4)	10.6 (±2.1)	8.7 (±2.2)	<0.001
E to Em ratio	6.9 (±2.3)	6.8 (±1.9)	7.1 (±2.8)	0.548
LV end-diastolic dimension (mm)	45 (±5)	45 (±5)	44 (±5)	0.342
Relative wall thickness	0.43 (±0.10)	0.42 (±0.08)	0.46 (±0.12)	0.062
LV mass index (gram/m²)	34 (±8)	34 (±7)	35 (±9)	0.416
Left atrial dimension (mm)	37 (±6)	37 (±6)	37 (±5)	0.906
Six-minute walk test				
Distance completed at 3 minutes (feet)	542 (±113)	563 (±119)	512 (±98)	0.035
Total distance completed at 6 minutes (feet)	1081 (±226)	1128 (±234)	1012 (±198)	0.017
Symptoms during walk	10 (11%)	8 (15%)	2 (6%)	0.162

Table 3

Associations of left ventricular diastolic dysfunction with six-minute walk test

	Correlation coefficient (R);	p value
Model 1: Unadjusted	−0.25	0.017
Model 2a: Model 1 plus cardiovascular morbidity	−0.35	0.048
Model 2b: Model 1 plus age	−0.32	0.105
Model 3: Model 1 plus age and cardiovascular morbidity	−0.38	0.161
Model 4: Model 3 plus sex, race, body mass index and systolic blood pressure	−0.44	0.365