Published in final edited form as:

J Aging Phys Act. 2013 October ; 21(4): 417–432.

Left Atrial Enlargement and Reduced Physical Function During Aging

Andrew A. Pellett, Leann Myers, Michael Welsch, S. Michal Jazwinski, and David A. Welsh

Pellett is with the Dept. of Cardiopulmonary Science, and Welsh, the Dept. of Medicine, Louisiana State University Health Sciences Center, New Orleans, LA. Myers is with the Dept. of Biostatistics and Bioinformatics, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA. Welsch is with the Dept. of Kinesiology, Louisiana State University, Baton Rouge, LA. Jazwinski is with the Tulane Center for Aging and Dept. of Medicine, Tulane University Health Sciences Center, New Orleans, LA

Abstract

Diastolic dysfunction, often seen with increasing age, is associated with reduced exercise capacity and increased mortality. Mortality rates in older individuals are linked to the development of disability, which may be preceded by functional limitations. The goal of this study was to identify which echocardiographic measures of diastolic function correlate with physical function in older subjects. A total of 36 men and women from the Louisiana Healthy Aging Study, age 62–101 yr, received a complete echocardiographic exam and performed the 10-item continuous-scale physical-functional performance test (CS-PFP-10). After adjustment for age and gender, left atrial volume index ($\rho = -0.59$; $p = .0005$) correlated with the total CS-PFP-10 score. Increased left atrial volume index may be a marker of impaired performance of activities of daily living in older individuals.

Keywords

diastolic function; left atrial volume; echocardiography; elderly; diastolic dysfunction

As a consequence of aging, the left ventricle (LV) typically develops diastolic dysfunction, defined as reduced LV relaxation and/or increased stiffness, while maintaining a normal ability to contract (systolic function; Abhayaratna, Marwick, Smith, & Becker, 2006; Redfield et al., 2003). Diastolic dysfunction is a frequent cause of symptoms in heart failure (Zile, Baicu, & Gaasch, 2004) and is associated with increased mortality (Halley, Houghtaling, Khalil, Thomas, & Jaber, 2011). Moreover, diastolic function appears to correlate with exercise capacity better than systolic function in middle-aged and older patients with heart failure (Gardin et al., 2009; Yoshino, Nakae, Matsumoto, Mitsunami, & Horie, 2010).

Decreases in LV relaxation or compliance can increase LV end-diastolic pressure (LVEDP), left atrial pressure, and, over time, left atrial volume (Pritchett et al., 2005; Tsang, Barnes, Gersh, Bailey, & Seward, 2002). Left atrial volume may increase as a result of normal aging (Aurigemma et al., 2009; Boyd, Schiller, Leung, Ross, & Thomas, 2011; Triposkiadis et al., 1995) and as a consequence of cardiovascular disease (Gottdiener, Kitzman, Aurigemma,

Arnold, & Manolio, 2006; Pritchett et al., 2003). Left atrial enlargement correlates with decreased exercise capacity (Kjaergaard et al., 2005; Wong & Yeo, 2010), increased risk of cardiovascular events (Leung et al., 2010; Pritchett et al., 2003), and a poor prognosis (Leung et al., 2010; Moller et al., 2003; Rossi et al., 2002).

According to the “disablement process” (Verbrugge & Jette, 1994), functional limitations resulting from pathologic impairment contribute to early disability and loss of independence. Subsequently, mortality rates are closely linked to disability in older individuals (Landi et al., 2010). The presumption, therefore, is that diastolic dysfunction may lead to physical limitations, which, in turn, contribute to disability. However, insufficient data are available to confirm the pathway linking diastolic heart function with a reduced ability to perform tasks involving physical function.

Diastolic dysfunction can be diagnosed by obtaining thinly sliced images of the heart with ultrasound (two-dimensional echocardiography) and by measuring cardiac blood flow and tissue velocities with Doppler echocardiography. Measures of diastolic function obtained with echocardiography include left atrial volume, LV inflow velocities associated with rapid filling (E velocity) and atrial contraction (A velocity), E-velocity deceleration time, mitral annular velocities during rapid LV filling (e') and atrial contraction (a'), and atrial contraction reversal velocity obtained in the right superior pulmonary vein (Nagueh et al., 2009).

The purpose of our study was to identify the echocardiographic diastolic function variables, specifically those related to elevated LVEDP, that correlate with physical function in subjects age 60 years and older. We hypothesized that an increase in left atrial volume would be associated with a reduction in physical performance involving everyday tasks, as measured by the 10-item continuous-scale physical-functional performance test (CS-PFP-10).

Methods

Participants

The Louisiana Healthy Aging Study (LHAS) was a community-based study conducted in the greater Baton Rouge area from 2002 to 2008. The overarching aim of LHAS was to determine the genetic, physiologic, and metabolic characteristics that predispose individuals to healthy aging. In the parent study, population-based sampling was performed via random selection using voter-registration lists and Medicare beneficiary enrollment data files from the Centers for Medicare and Medicaid Services. Nonagenarians were oversampled as the experimental group, with control subjects ranging from age 25 to 89. The study was approved by the institutional review boards of the involved institutions, and informed written consent obtained.

Subjects included in this analysis represent the subset of LHAS participants over the age of 59 who underwent digital echocardiographic assessment and also performed the CS-PFP-10. Exclusion criteria consisted of active atrial fibrillation and a calculated mitral valve area of less than 1.5 cm².

Medical History and Physical Exam

Medical history was recorded by interview using a standardized instrument. Weight was measured to ± 0.1 kg with an electronic scale (Detecto, Webb City, MO). Height was measured to ± 0.5 cm with a wall-mounted stadiometer (Holtain, Crymych, Dyfed, UK), and body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Blood pressure was measured in a quiet room with minimal temperature fluctuations after a 5-min rest period. All measurements were taken twice (and averaged) on the participant's right arm with a manual sphygmomanometer (Baum, Coplaque, NY).

Echocardiography

All echocardiograms were performed by the same experienced registered cardiac sonographer using a Toshiba Aplio echocardiograph (Toshiba America Medical Systems, Tustin, CA). Two-dimensional color-flow Doppler and spectral Doppler echocardiography were used to screen for valvular disease. Echocardiographic variables were measured in triplicate and averaged.

LV and left atrial volumes were measured with the biplane method of disks (Khankirawatana, Khankirawatana, & Porter, 2004; Schiller et al., 1989). Briefly, this method involves imaging each chamber in two orthogonal planes. Both images of a chamber are then divided into 20 slices. The area of each slice is calculated, and by combining the two images and then measuring the length of the chamber and dividing by 20, the volume of each presumed elliptical disk can be calculated. Summing the volumes of the 20 disks yields the volume of the chamber. Measuring the volume of the LV at end-diastole and end-systole permits the calculation of ejection fraction (EF), a common clinical measure of ventricular systolic function: $\text{EF} = (\text{end-diastolic volume} - \text{end-systolic volume}) / \text{end-diastolic volume}$.

Using two-dimensional linear measurements, LV mass was calculated with an equation that modeled the LV as a prolate ellipse (Devereux et al., 1986). LV mass, as well as LV end-diastolic and left atrial volumes, was indexed to body surface area.

Echocardiographic diastolic function variables were obtained according to previous recommendations (Appleton, Jensen, Hatle, & Oh, 1997; Hill & Palma, 2005). A 1-mm pulsed Doppler sample volume was positioned at the mitral leaflet tips in the apical four-chamber view to record mitral inflow E and A velocities and E-wave deceleration time. Mitral A-wave duration was measured after advancing the sample volume toward the level of the mitral annulus. In the same view, mitral lateral and septal annular e' and a' velocities were measured by sequentially placing 5-mm and 3-mm pulsed Doppler sample volumes, respectively, at the lateral and septal aspects of the mitral annulus. The mitral E velocity was divided by e' velocity obtained from the lateral mitral annulus to yield E/e' , a measure of LV filling pressure. Pulmonary venous velocity waveforms were obtained in the apical four-chamber view by advancing a 5-mm pulsed Doppler sample volume 0.5–1 cm into the right superior pulmonary vein. From these traces pulmonary venous systolic and diastolic peak velocities were measured, as well as atrial reversal wave velocity and duration. The criteria for the diagnosis of diastolic dysfunction consisted of a mitral $E:A < 0.75$ combined with a

deceleration time >240 ms, a mitral lateral e' velocity <10 cm/s, or a mitral septal e' velocity <8 cm/s (Nagueh et al., 2009; Redfield et al., 2003).

Measure of Physical Function

The measure of physical function used in our analysis was the CS-PFP-10 (Cress, Petrella, Moore, & Schenkman, 2005). Briefly, the CS-PFP-10 involves the performance of 10 standardized tasks representing activities of daily living, including carrying groceries, donning clothes, sweeping the floor, unloading a washer and loading a dryer, climbing stairs, and a 6-min timed walk. Participants are instructed to perform the activities at peak effort but within the bounds of safety and comfort. The time required to complete the tasks, distance covered, and/or weight carried are compiled and converted to a set of continuous-scale scores ranging from 0 to 100. The test battery provides scores in five physical domains (balance and coordination, endurance, upper body flexibility, and upper and lower body strength) and a summed total score. Details of the scoring method can be found elsewhere (Cress et al., 1999). The CS-PFP-10, which is a shortened version of the Continuous-Scale Physical Functional Performance Test developed by Cress et al. (1996), has been shown to be valid, reliable, and sensitive and a good community-based substitute for the original 16-item laboratory test (Cress et al., 2005).

Statistics

Data were summarized using means and standard deviations. Associations between echocardiographic and physical-performance variables were assessed using partial Spearman rho correlation coefficients, and the Bonferroni method was used to correct for multiple comparisons. All analyses were conducted using SAS version 9.2.

Results

Thirty-six subjects received both echocardiographic and CS-PFP-10 evaluations. Left atrial volume index (LAVI) could not be measured in 4 individuals due to poor image quality, nor could EF in 3 of the same subjects. Pulmonary venous waveforms could not be measured adequately in 7 individuals. Subject characteristics are presented in Table 1, and echocardiographic and CS-PFP-10 data for the study population are presented in Tables 2 and 3, respectively.

Of the 32 subjects in whom LAVI was measured, 24 exhibited at least mild atrial enlargement (LAE), defined as $LAVI > 28 \text{ ml/m}^2$ (Lang et al., 2005). The subjects with LAE included 17 with diastolic dysfunction, 7 with coronary artery disease, and 5 with diabetes. Eight of the subjects with LAE had a history of heart failure, but only 3 exhibited a reduced EF (<50%) at the time of the echocardiogram. Twenty-one of the 32 subjects (66%) exhibited diastolic dysfunction, 17 of whom (81%) had LAE.

Correlations between echocardiographic variables related to LVEDP and the total CS-PFP-10 score were assessed. After adjustment for age and gender, LAVI was found to correlate inversely with the total CS-PFP-10 score, as well as with all domains. After adjustment for multiple comparisons, however, LAVI only correlated significantly with the total CS-PFP-10 score and the endurance domain (Figure 1; Table 4). Pulmonary venous

atrial reversal velocity was directly associated with the total CS-PFP-10 score but did not correlate significantly after Bonferroni adjustment. The following echocardiographic variables did not correlate significantly with the total CS-PFP-10 score: mitral E-to-A ratio ($\rho = -0.2$, $p = .27$, $n = 36$), mitral *a*-wave duration ($\rho = -0.34$, $p = .08$, $n = 30$), deceleration time ($\rho = 0.11$, $p = .53$, $n = 35$), atrial reversal wave duration ($\rho = 0.20$, $p = .32$, $n = 28$), mitral E/e' ($\rho = 0.12$, $p = .51$, $n = 36$), and LV mass index ($\rho = -0.27$, $p = .12$, $n = 36$).

Discussion

Using a unique, observer-assessed measure of functional ability, the analyses appear to be consistent with the model in which left atrial dilation affects the performance of activities of daily living. Note that LAVI was identified as a primary echocardiographic metric relevant to the disablement process described by Verbrugge and Jette (1994).

Diastolic Function, Left Atrial Volume, and Aging

Redfield et al. (2003) found that the prevalence of diastolic dysfunction increased with age in a large-scale survey of randomly selected residents of Olmstead County, Minnesota, age 45 years and older. In the oldest age group in that study (75 years), diastolic dysfunction was found in almost 71% of the subjects. In a similar survey of residents of Canberra, Australia, the prevalence of diastolic dysfunction in subjects 80–86 years of age was about 64% (Abhayaratna et al., 2006). A relationship between left atrial volume and normal aging has been shown in some studies (Aurigemma et al., 2009; Boyd et al., 2011; Triposkiadis et al., 1995) and contradicted by others (Pritchett et al., 2003; Thomas et al., 2002). Previous population-based surveys of middle-aged to elderly segments of the population have shown an association of LAE with cardiovascular disease prevalence (Gottdiener et al., 2006; Pritchett et al., 2003). Twenty-one of the 36 subjects (61%) in the current study exhibited diastolic dysfunction, while LAE was identified in 71% of the 32 subjects in whom left atrial volume was measured. We are not aware of any studies examining diastolic function in a cohort that includes a relatively high percentage of nonagenarians, with or without cardiovascular disease. Given the strong association of cardiovascular disease prevalence with advanced age, it is extremely difficult to obtain a sizeable cohort of nonagenarians without a history of hypertension or heart disease. Because we did not exclude subjects with such a history, our results do not permit us to make definitive conclusions regarding the effects of nonpathological aging. It is likely that our findings represent a combination of the normal aging process and the superimposition of conditions such as coronary artery disease and hypertension, both of which may cause diastolic dysfunction (Hoffmann et al., 2010; Pavlopoulos et al., 2008).

Diastolic Function and Physical Function

Diastolic dysfunction has been shown to contribute to exercise intolerance in patients with heart failure and normal or decreased systolic function (Gardin et al., 2009; Haykowsky et al., 2011; Kitzman, Higginbotham, Cobb, Sheikh, & Sullivan, 1991; Meyer, Karamanoglu, Ehsani, & Kovacs, 2004; Parthenakis et al., 2000), perhaps due to an increase in LV filling pressures (Packer, 1990). Grewal, McCully, Kane, Lam, and Pellikka (2009) measured diastolic function in a large group of patients referred for exercise echocardiography,

excluding individuals with significant valvular disease, an EF <50%, and exercise-induced myocardial ischemia. They found that the grade of diastolic dysfunction, which included measurements of mitral E/A, e', and E/e', as well as left atrial volume, exhibited the strongest association with exercise capacity. Resting mitral E/e', an indicator of increased filling pressures (Ommen et al., 2000), has been shown to correlate negatively with exercise capacity (Eroglu et al., 2011; Hadano et al., 2006; Skaluba & Litwin, 2004). In a convenience sample of community-dwelling older adults without a history of heart failure, Perry et al. (2011) found that 6-min-walk distances in subjects 65 years old correlated inversely with the early (E) to atrial (A) transmitral peak inflow velocity ratios and early mitral annular velocities. However, the correlation lost significance after adjustment for age, body-mass index, and cardiovascular morbidity. The current study did not demonstrate a significant relationship between CS-PFP-10 score and mitral lateral E/e'. This finding may be related to the somewhat inhomogeneous nature of our subject population, as the ability of E/e' to predict filling pressures in patients with reduced EF has recently been questioned (Mullens, Borowski, Curtin, Thomas, & Tang, 2009; Tschope & Paulus, 2009). In addition, the presence of chronic increases in filling pressure may be better reflected by left atrial volume, as opposed to E/e', which is more affected by transient alterations in left atrial pressure.

LAE and Physical Function

Chronic elevation of LV filling pressures, which may be caused by diastolic dysfunction, increases left atrial volume (Tsang et al., 2002). Increased LAVI has been shown to be an independent predictor of reduced exercise capacity in patients with isolated diastolic dysfunction (Wong & Yeo, 2010) and hypertrophic cardiomyopathy (Kjaergaard et al., 2005). In addition, LAVI determines prognosis in a wide variety of cardiovascular conditions (Leung et al., 2010; Rossi et al. 2002; Sakaguchi et al., 2011). Recently, Tan et al. (2010) demonstrated that impaired left atrial function may contribute to exercise intolerance in patients with heart failure and normal EF. Only about 28% of the subjects in the current study reported a history of heart failure, with about 90% having a normal EF. A majority of the subjects exhibited left atrial enlargement and echocardiographic signs of diastolic dysfunction. It is difficult to say how a larger LAVI may be linked to lower physical function in our cohort. We speculate that increased LAVI and LV filling pressures may contribute to a lower stroke volume, with a subsequent greater reliance on heart rate to perform certain physical tasks. We did not monitor heart rate during the CS-PFP-10 but theorize that the individuals with higher LAVI may have had higher heart-rate responses, which may have contributed to earlier fatigue. It is particularly interesting that the strongest identified association was between LAVI and endurance, which is largely defined by the 6-min-walk test, the last test in the CS-PFP-10 battery.

To our knowledge, ours is the first study to associate LAVI with a quantitative measure of physical performance involving everyday tasks. We used the CS-PFP-10 in place of the original laboratory-based Continuous-Scale Physical-Functional Performance Test, which has been shown to correlate with reduced aerobic reserve in older subjects (Arnett, Laity, Agrawal, & Cress, 2008), as well as with task modification in individuals with preclinical disability (Petrella & Cress, 2004). Our results suggest that left atrial dilation may act as an

intermediary (“impairment”) in the disablement process linking pathology to functional limitations, which results in a predisposition to disability. Due to the association with lower scores on the CS-PFP-10, increased LAVI could potentially function as a marker of increased risk of loss of independence in individuals over the age of 65 (Cress & Meyer, 2003). Recently, Leibowitz et al. (2011) reported that 85- and 86-year-olds requiring assistance with at least one activity of daily living (dependent) were likely to have higher LAVI and LV mass index, along with a lower EF, than independent subjects of the same age. Consistent with the results of the current study, no Doppler measures of diastolic function differed between the dependent and independent groups. It is not yet clear what interventions, if any, may be effective in reducing left atrial volume, although it would presumably involve a resolution of the structural myocardial abnormalities that accompany diastolic dysfunction, such as concentric hypertrophy and increased LV stiffness. Clinical trials in patients with heart failure and normal EF have thus far failed to demonstrate a benefit of angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and beta-blockers (Paulus & van Ballegoij, 2010). There is recent evidence that exercise training improves diastolic function in patients with heart failure with preserved EF (Edelmann et al., 2011), perhaps secondary to improved calcium kinetics (Petrella, Cunningham, & Paterson, 2000).

Limitations

Due to the cross-sectional design of this study, we are limited in our ability to identify cause-and-effect relationships. The small sample size also reduced our ability to control for all confounding variables, making it difficult to establish a direct link between diastolic dysfunction and left atrial enlargement. An EF <50%, which we did not include as a covariate, may contribute to increases in left atrial volume, although this form of systolic dysfunction was only present in about 9% of the subjects, whereas over 60% exhibited evidence of diastolic dysfunction and >80% of those subjects demonstrated LAE. Mitral regurgitation, which may also increase left atrial volume, was also not a covariate. However, only 3 subjects in whom LAVI was measured exhibited more than mild mitral regurgitation, none of which was severe. In addition, the extrapolation of our results to younger cohorts may not be valid due to the high percentage of octogenarian and nonagenarian subjects in our study. Despite these limitations, we were able to identify a relatively strong association (compared with similar correlational studies in the literature) between LAVI and physical performance. Longitudinal studies involving a greater number of subjects should be performed to better characterize the role of left atrial volume and function (and perhaps other variables) in exceptional longevity.

Conclusions

In a cross-sectional population-based survey examining echocardiographic variables of diastolic function, we demonstrated a significant association between increased LAVI and decreased total and endurance domain scores of the CS-PFP-10. This is consistent with the idea that some form of impairment (left atrial dilation) contributes to a loss of physical function, which in turn leads to disability (the disablement process).

Acknowledgments

The authors would like to thank the following individuals for their work with the Louisiana Healthy Aging Study:

Meghan B. Allen, Gloria Anderson, Iina E. Antikainen, Arturo M. Arce, Jennifer Arceneaux, Mark A. Batzer, Xiuhua Bi, Emily O. Boudreaux, Lauri Byerley, Pauline Callinan, Catherine M. Champagne, Hau Cheng, Katie E. Cherry, Yu-Wen Chiu, Liliana Cosenza, M. Elaine Cress, Jianliang Dai, James P. DeLany, W. Andrew Deutsch, Melissa J. deVeer, Devon A. Dobrosielski, Rebecca Ellis, Andrea Ermolao, Marla J. Erwin, Mark Erwin, Jennifer M. Fabre, Elizabeth T.H. Fontham, Madlyn Frisard, Paula Geiselman, Lindsey Goodwin, Sibte Hadi, Tiffany Hall, Michael Hamilton, Scott W. Herke, Karri S. Hawley, Jennifer Hayden, Kristi Hebert, Fernanda Holton, Hui-Chen Hsu, Darcy Johannsen, Lumie Kawasaki, Darla Kendzor, Sangkyu Kim, Beth G. Kimball, Christina King-Rowley, Miriam Konkell, Robyn Kuhn, Kim Landry, Carl Lavie, Daniel LaVie, Matthew Leblanc, Li Li, Hui-Yi Lin, Kay Lopez, Bridget McEvoy-Hein, John D. Mountz, Jennifer Owens, Kim B. Pedersen, Eric Ravussin, Paul Remedios, Yolanda Robertson, Jennifer Rood, Henry Rothschild, Ryan A. Russell, Erin Sandifer, Beth Schmidt, Robert Schwartz, Donald K. Scott, Mandy Shipp, Jennifer L. Silva, F. Nicole Standberry, Abha Tiwari, Mary Susan Thomas, Jessica Thomson, Valerie Toups, Cruz Velasco-Gonzalez, Julia Volaufova, Celeste Waguespack, Jerilyn A. Walker, Xiu-Yun Wang, Robert H. Wood, Qingzhao Yu, Sarah Zehr, Pili Zhang.

Louisiana State University, Baton Rouge; Ochsner Clinic Foundation, New Orleans; Pennington Biomedical Research Center, Baton Rouge; Louisiana State University Health Sciences Center, New Orleans; Tulane University, New Orleans; University of Alabama, Birmingham; University of Colorado, Aurora; University of Georgia, Athens, United States.

Supported by grants from the National Institute on Aging of the National Institutes of Health (P01 AG022064) and by the Louisiana Board of Regents through the Millennium Trust Health Excellence Fund (HEF[2001-06]-02).

References

- Abhayaratna WP, Marwick TH, Smith WT, Becker NG. Characteristics of left ventricular diastolic dysfunction in the community: An echocardiographic survey. *Heart (British Cardiac Society)*. 2006; 92:1259–1264.10.1136/hrt.2005.080150 [PubMed: 16488928]
- Appleton CP, Jensen JL, Hatle LK, Oh JK. Doppler evaluation of left and right ventricular diastolic function: A technical guide for obtaining optimal flow velocity recordings. *Journal of the American Society of Echocardiography*. 1997; 10:271–292.10.1016/S0894-7317(97)70063-4 [PubMed: 9109692]
- Arnett SW, Laity JH, Agrawal SK, Cress ME. Aerobic reserve and physical functional performance in older adults. *Age and Ageing*. 2008; 37:384–389.10.1093/ageing/afn022 [PubMed: 18287178]
- Aurigemma GP, Gottdiener JS, Arnold AM, Chinali M, Hill JC, Kitzman D. Left atrial volume and geometry in healthy aging: The Cardiovascular Health Study. *Circulation: Cardiovascular Imaging*. 2009; 2:282–289.10.1161/CIR-CIMAGING.108.826602 [PubMed: 19808608]
- Boyd AC, Schiller NB, Leung D, Ross DL, Thomas L. Atrial dilation and altered function are mediated by age and diastolic function but not before the eighth decade. *JACC: Cardiovascular Imaging*. 2011; 4:234–242.10.1016/j.jcmg.2010.11.018 [PubMed: 21414570]
- Cress ME, Buchner DM, Questad KA, Esselman PC, deLateur BJ, Schwartz RS. Continuous-scale physical functional performance in healthy older adults: A validation study. *Archives of Physical Medicine and Rehabilitation*. 1996; 77:1243–1250.10.1016/S0003-9993(96)90187-2 [PubMed: 8976306]
- Cress ME, Buchner DM, Questad KA, Esselman PC, deLateur BJ, Schwartz RS. Exercise: Effects on physical functional performance in independent older adults. *The Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 1999; 54:M242–M248. PubMed.
- Cress ME, Meyer M. Maximal voluntary and functional performance levels needed for independence in adults aged 65 to 97 years. *Physical Therapy*. 2003; 83:37–48. PubMed. [PubMed: 12495411]
- Cress ME, Petrella JK, Moore TL, Schenkman ML. Continuous-scale physical functional performance test: Validity, reliability, and sensitivity of data for the short version. *Physical Therapy*. 2005; 85:323–335. PubMed. [PubMed: 15794703]
- Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: Comparison to necropsy findings. *The American Journal of Cardiology*. 1986; 57:450–458.10.1016/0002-9149(86)90771-X [PubMed: 2936235]

- Edelmann F, Gelbrich G, Dungen HD, Frohling S, Wachter R, Stahrenberg R, et al. Pieske B. Exercise training improves exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction. Results of the Ex-DHF (Exercise Training in Diastolic Heart Failure) pilot study. *Journal of the American College of Cardiology*. 2011; 58:1780–1791.10.1016/j.jacc.2011.06.054 [PubMed: 21996391]
- Eroglu S, Sade LE, Aydinalp A, Yildirim A, Bozbas H, Ulubay G, Muderrisoglu H. Association between cardiac functional capacity and parameters of tissue Doppler imaging in patients with normal ejection fraction. *Acta Cardiologica*. 2011; 66:181–187.10.2143/AC.66.2.2071249 [PubMed: 21591576]
- Gardin JM, Leifer ES, Fleg JL, Whellan D, Kokkinos P, LeBlanc MH, et al. Kitzman DW. Relationship of Doppler-echocardiographic left ventricular diastolic function to exercise performance in systolic heart failure: The HF-ACTION study. *American Heart Journal*. 2009; 158:S45–S52.10.1016/j.ahj.2009.07.015 [PubMed: 19782788]
- Gottdiener JS, Kitzman DW, Aurigemma GP, Arnold AM, Manolio TA. Left atrial volume, geometry, and function in systolic and diastolic heart failure of persons ≥ 65 years of age (The Cardiovascular Health Study). *The American Journal of Cardiology*. 2006; 97:83–89.10.1016/j.amjcard.2005.07.126 [PubMed: 16377289]
- Grewal J, McCully RB, Kane GC, Lam C, Pellicka PA. Left ventricular function and exercise capacity. *Journal of the American Medical Association*. 2009; 301(3):286–294.10.1001/jama.2008.1022 [PubMed: 19155455]
- Hadano Y, Murata K, Tamamoto T, Kunichika H, Matsumoto T, Akagawa E, et al. Matsuzaki M. Usefulness of mitral annular velocity in predicting exercise tolerance in patients with impaired left ventricular systolic function. *The American Journal of Cardiology*. 2006; 97:1025–1028.10.1016/j.amjcard.2005.10.044 [PubMed: 16563909]
- Halley CM, Houghtaling PL, Khalil MK, Thomas JD, Jaber WA. Mortality rate in patients with diastolic dysfunction and normal systolic function. *Archives of Internal Medicine*. 2011; 171(12): 1082–1087.10.1001/archinternmed.2011.244 [PubMed: 21709107]
- Haykowsky MJ, Brubaker PH, John JM, Stewart KP, Morgan TM, Kitzman DW. Determinants of exercise capacity in elderly heart failure patients with preserved ejection fraction. *Journal of the American College of Cardiology*. 2011; 58:265–274.10.1016/j.jacc.2011.02.055 [PubMed: 21737017]
- Hill JC, Palma RA. Doppler tissue imaging for the assessment of left ventricular diastolic function: A systematic approach for the sonographer. *Journal of the American Society of Echocardiography*. 2005; 18:80–88.10.1016/j.echo.2004.09.007 [PubMed: 15637496]
- Hoffmann S, Mogelvang R, Olsen NT, Sogaard P, Fritz-Hansen T, Bech J, et al. Jensen JS. Tissue Doppler echocardiography reveals distinct patterns of impaired myocardial velocities in different degrees of coronary artery disease. *European Journal of Echocardiography*. 2010; 11:544–549.10.1093/ejehocard/jeq015 [PubMed: 20207722]
- Khankirawatana B, Khankirawatana S, Porter T. How should left atrial size be reported? Comparative assessment with use of multiple echocardiographic methods. *American Heart Journal*. 2004; 147:369–374.10.1016/j.ahj.2003.03.001 [PubMed: 14760338]
- Kitzman DW, Higginbotham MB, Cobb FR, Sheikh KH, Sullivan MJ. Exercise intolerance in patients with heart failure and preserved left ventricular systolic function: Failure of the Frank-Starling mechanism. *Journal of the American College of Cardiology*. 1991; 17:1065–1072.10.1016/0735-1097(91)90832-T [PubMed: 2007704]
- Kjaergaard J, Johnson BD, Pellicka PA, Cha SS, Oh JK, Ommen SR. Left atrial index is a predictor of exercise capacity in patients with hypertrophic cardiomyopathy. *Journal of the American Society of Echocardiography*. 2005; 18:1373–1380.10.1016/j.echo.2005.05.020 [PubMed: 16376769]
- Landi F, Liperoti R, Russo A, Capoluongo E, Barillaro C, Pahor M, et al. Onder G. Disability, more than multimorbidity, was predictive of mortality among older persons aged 80 years and older. *Journal of Clinical Epidemiology*. 2010; 63:752–759.10.1016/j.jclinepi.2009.09.007 [PubMed: 20056387]
- Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellicka PA, et al. Sutton MS. Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing

- Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *Journal of the American Society of Echocardiography*. 2005; 18:1440–1463.10.1016/j.echo.2005.10.005 [PubMed: 16376782]
- Leibowitz D, Jacobs JM, Stessman-Lande I, Cohen A, Gilon D, Ein-Mor E, Stessman J. Cardiac structure and function and dependency in the oldest old. *Journal of the American Geriatrics Society*. 2011; 59:1429–1434.10.1111/j.1532-5415.2011.03534.x [PubMed: 21824119]
- Leung DY, Chi C, Allman C, Boyd A, Ng AC, Kadappu KK, et al. Thomas L. Prognostic implications of left atrial volume index in patients in sinus rhythm. *The American Journal of Cardiology*. 2010; 105:1635–1639.10.1016/j.amj-card.2010.01.027 [PubMed: 20494675]
- Meyer TE, Karamanoglu M, Ehsani AA, Kovacs SJ. Left ventricular chamber stiffness at rest as a determinant of exercise capacity in heart failure subjects with decreased ejection fraction. *Journal of Applied Physiology*. 2004; 97:1667–1672.10.1152/japplphysiol.00078.2004 [PubMed: 15208299]
- Moller JE, Hillis GS, Oh JK, Seward JB, Reeder GS, Wright RS, et al. Pellikka PA. Left atrial volume. A powerful predictor of survival after acute myocardial infarction. *Circulation*. 2003; 107:2207–2212.10.1161/01.CIR.0000066318.21784.43 [PubMed: 12695291]
- Mullens W, Borowski AG, Curtin RJ, Thomas JD, Tang WH. Tissue Doppler imaging in the estimation of intracardiac filling pressure in decompensated patients with advanced systolic heart failure. *Circulation*. 2009; 119:62–70.10.1161/CIRCULATIONAHA.108.779223 [PubMed: 19075104]
- Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Evangelista A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Journal of the American Society of Echocardiography*. 2009; 22:107–133.10.1016/j.echo.2008.11.023 [PubMed: 19187853]
- Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. *Circulation*. 2000; 102:1788–1794.10.1161/01.CIR.102.15.1788 [PubMed: 11023933]
- Packer M. Abnormalities of diastolic function as a potential cause of exercise intolerance in chronic heart failure. *Circulation*. 1990; 81(Suppl.):III-78–III-86. PubMed. [PubMed: 1967559]
- Parthenakis FI, Kanoupakis EM, Kochiadakis GE, Skolidis EI, Mezilis NE, Siman-tirakis EN, et al. Vardas PE. Left ventricular diastolic filling pattern predicts cardiopulmonary determinants of functional capacity in patients with congestive heart failure. *American Heart Journal*. 2000; 140:338–344.10.1067/mhj.2000.108243 [PubMed: 10925352]
- Paulus WJ, van Ballegoij JJM. Treatment of heart failure with normal ejection fraction. An inconvenient truth! *Journal of the American College of Cardiology*. 2010; 55:526–537.10.1016/j.jacc.2009.06.067 [PubMed: 20152557]
- Pavlopoulos H, Grapsa J, Stefanadi E, Kamperidis V, Philippou E, Dawson D, Nihoyannopoulos P. The evolution of diastolic function in the hypertensive disease. *European Journal of Echocardiography*. 2008; 9:772–778.10.1093/ejehocard/jen145 [PubMed: 18490288]
- Perry GJ, Ahmed MI, Desai RV, Mujib M, Zile M, Sui X, et al. Ahmed A. Left ventricular diastolic function and exercise capacity in community-dwelling adults 65 years of age without heart failure. *The American Journal of Cardiology*. 2011; 108:735–740.10.1016/j.amjcard.2011.04.025 [PubMed: 21704282]
- Petrella JK, Cress ME. Daily ambulation activity and task performance in community-dwelling older adults aged 63–71 years with preclinical disability. *The Journals of Gerontology Series A, Biological Sciences and Medical Sciences*. 2004; 59:264–267.10.1093/gerona/59.3.M264
- Petrella RJ, Cunningham DA, Paterson DH. Left ventricular filling and cardiovascular functional capacity in older men. *Experimental Physiology*. 2000; 85:547–555.10.1017/S0958067000020261 [PubMed: 11038406]
- Pritchett AM, Jacobsen SJ, Mahoney DW, Rodeheffer RJ, Bailey KR, Redfield MM. Left atrial volume as an index of left atrial size: A population-based study. *Journal of the American College of Cardiology*. 2003; 41:1036–1043.10.1016/S0735-1097(02)02981-9 [PubMed: 12651054]

- Pritchett AM, Mahoney DW, Jacobsen SJ, Rodeheffer RJ, Karon BL, Redfield MM. Diastolic dysfunction and left atrial volume. A population-based study. *Journal of the American College of Cardiology*. 2005; 45:87–92.10.1016/j.jacc.2004.09.054 [PubMed: 15629380]
- Redfield MM, Jacobsen SJ, Burnett JC, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community. Appreciating the scope of the heart failure epidemic. *Journal of the American Medical Association*. 2003; 289:194–202.10.1001/jama.289.2.194 [PubMed: 12517230]
- Rossi A, Ciccoira M, Zanolli L, Sandrini R, Golia G, Zardini P, Enriquez-Sarano M. Determinants and prognostic value of left atrial volume in patients with dilated cardiomyopathy. *Journal of the American College of Cardiology*. 2002; 40:1425–1430.10.1016/S0735-1097(02)02305-7 [PubMed: 12392832]
- Sakaguchi E, Yamada A, Sugimoto K, Ito Y, Shiino K, Takada K, et al. Ozaki Y. Prognostic value of left atrial volume index in patients with first acute myocardial infarction. *European Journal of Echocardiography*. 2011; 12:440–444.10.1093/ejehocard/er058 [PubMed: 21586536]
- Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Tajik AJ. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *Journal of the American Society of Echocardiography*. 1989; 2:358–367. PubMed. [PubMed: 2698218]
- Skaluba SJ, Litwin SE. Mechanisms of exercise intolerance. Insights from tissue Doppler imaging. *Circulation*. 2004; 109:972–977. doi:10.1161/01.CIR.0000117405.74491. D2. [PubMed: 14967722]
- Tan YT, Wenzelburger F, Lee E, Nightingale P, Heatlie G, Leyva F, Sanderson JE. Reduced left atrial function on exercise in patients with heart failure and normal ejection fraction. *Heart (British Cardiac Society)*. 2010; 96:1017–1023.10.1136/hrt.2009.189118 [PubMed: 20584857]
- Thomas L, Levett K, Boyd A, Leung DYC, Schiller NB, Ross DL. Compensatory changes in atrial volumes with normal aging: Is atrial enlargement inevitable? *Journal of the American College of Cardiology*. 2002; 40:1630–1635.10.1016/S0735-1097(02)02371-9 [PubMed: 12427416]
- Triposkiadis F, Tentolouris K, Androulakis A, Trikas A, Toutouzas K, Kyriakidis M, et al. Toutouzas P. Left atrial mechanical function in the healthy elderly: New insights from a combined assessment of changes in atrial volume and transmitral flow velocity. *Journal of the American Society of Echocardiography*. 1995; 8:801–809.10.1016/S0894-7317(05)80004-5 [PubMed: 8611280]
- Tsang TSM, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. *The American Journal of Cardiology*. 2002; 90:1284–1289.10.1016/S0002-9149(02)02864-3 [PubMed: 12480035]
- Tschope C, Paulus WJ. Doppler echocardiography yields dubious estimates of left ventricular diastolic pressures. *Circulation*. 2009; 120:810–820.10.1161/CIRCULATIONAHA.109.869628 [PubMed: 19720947]
- Verbrugge LM, Jette AM. The disablement process. *Social Science & Medicine*. 1994; 38:1–14.10.1016/0277-9536(94)90294-1 [PubMed: 8146699]
- Wong RC, Yeo TC. Left atrial volume is an independent predictor of exercise capacity in patients with isolated left ventricular diastolic dysfunction. *International Journal of Cardiology*. 2010; 144:425–427.10.1016/j.ijcard.2009.03.060 [PubMed: 19356810]
- Yoshino T, Nakae I, Matsumoto T, Mitsunami K, Horie M. Relationship between exercise capacity and cardiac diastolic function assessed by time-volume curve from 16-frame gated myocardial perfusion SPECT. *Annals of Nuclear Medicine*. 2010; 24:469–476.10.1007/s12149-010-0382-x [PubMed: 20458562]
- Zile MR, Baicu CF, Gaasch WH. Diastolic heart failure—Abnormalities in active relaxation and passive stiffness of the left ventricle. *The New England Journal of Medicine*. 2004; 350(19):1953–1959.10.1056/NEJMoa032566 [PubMed: 15128895]

Figure 1.

Scatterplot of ranked values of left atrial volume index (LAVI) versus ranked values of total score on the 10-item continuous-scale physical-functional performance test (CS-PFP-10).

Table 1

Baseline Subject Characteristics

	Age Group						Overall, N = 36
	60–69, n = 2	70–79, n = 6	80–89, n = 12	≥90, n = 16			
Men, n	1	4	6	4		15	
Women, n	1	2	6	12		21	
SBP (mm Hg), <i>M</i> ± <i>SD</i>	132.5 ± 7.8	136.0 ± 7.3	146.2 ± 12.2	142.8 ± 18.9		142.4 ± 15.2	
DBP (mm Hg), <i>M</i> ± <i>SD</i>	66.5 ± 12.0	71.6 ± 8.6	73.3 ± 10.4	70.9 ± 7.4		71.6 ± 8.6	
Heart rate (beats/min), <i>M</i> ± <i>SD</i>	51.0 ± 1.4	71.7 ± 10.0	61.6 ± 11.5	66.8 ± 14.6		65.0 ± 13.1	
Cardiovascular history, n							
dysrhythmia	0	1	0	1		2	
high blood pressure	0	5	10	12		27	
heart failure	0	2	2	6		10	
CAD ^a	0	2	5	2		9	
atrial fibrillation	0	0	3	3		6	
diabetes	0	2	2	2		6	

Note. SBP = systolic blood pressure; DBP = diastolic blood pressure; CAD = coronary artery disease.

^aHistory of any of the following: heart attack, angina, angioplasty, coronary bypass surgery.

Table 2

Echocardiographic Variables ($M \pm SD$)

	Age Group				Range
	60-69	70-79	80-89	≥90	
EF	64.6 ^a	60.8 ± 17.6	61.8 ± 14.5	69.3 ± 10.5	26.2-89.0
E (m/s)	1.0 ± 0.2	0.9 ± 0.2	0.9 ± 0.1	1.1 ± 0.4	0.4-1.7
A (m/s)	1.0 ± 0.0	0.7 ± 0.4	0.9 ± 0.4	1.1 ± 0.4	0.2-1.9
E:A	1.1 ± 0.2	1.6 ± 1.1	1.5 ± 1.1	1.1 ± 0.8	0.4-3.7
A Dur (ms)	117.0 ^a	142.1 ± 25.3	135.2 ± 11.5	152.7 ± 13.3	114.0-187.7
DCT (ms)	186.5 ± 6.4	186.3 ± 34.8	212.2 ± 29.4	236.5 ± 68.4	135.5-369.7
Lateral e' (cm/s)	10.9 ± 0.8	10.9 ± 2.6	10.1 ± 2.6	9.4 ± 2.5	5.5-15.5
Septal e' (cm/s)	10.7 ± 0.4	9.0 ± 2.0	9.2 ± 2.5	8.5 ± 2.1	5.1-13.0
E:e'	9.5 ± 2.4	8.8 ± 2.3	9.7 ± 3.4	12.2 ± 5.0	4.8-22.1
PVAR (cm/s)	30.7 ± 5.1	30.4 ± 3.5	32.2 ± 5.7	29.2 ± 5.8	19.5-44.5
PVAR Dur (ms)	154.8 ± 22.4	152.1 ± 29.8	157.1 ± 24.3	154.8 ± 30.2	98.0-215.3
LAVI (ml/cm ²)	34.5 ^a	28.3 ± 7.4	36.9 ± 14.4	41.1 ± 14.3	7.1-68.2
LVMl (g/cm ²)	93.4 ± 9.3	94.1 ± 32.7	96.4 ± 26.6	105.9 ± 31.2	49.0-163.3

Note. EF = ejection fraction; E = mitral inflow velocity; A = atrial contraction velocity; E:A = ratio of E to A; A dur = duration of mitral A wave; DCT = left ventricular inflow deceleration time; lateral e' = left ventricular inflow velocity of lateral mitral annulus; Septal e' = ratio of E to lateral mitral annular inflow velocity; VA R = pulmonary venous atrial reversal velocity; PVAR Dur = duration of pulmonary venous atrial reversal velocity; LAVI = left atrial volume index; LVMl = left ventricular mass index.

^aNo standard deviation because $n = 1$ for this variable.

Table 3

CS-PFP-10 Scores ($M \pm SD$)

	Age Group						Overall, $N = 36$	Range
	60–69, $n = 2$	70–79, $n = 6$	80–89, $n = 12$	>90, $n = 16$				
Total CS-PFP-10	44.5 $\pm$ 58.6	45.5 $\pm$ 13.4	33.2 $\pm$ 12.7	20.3 $\pm$ 10.5			30.2 $\pm$ 17.9	3.0–85.9
Domain								
balance/coordination	44.5 $\pm$ 60.6	44.4 $\pm$ 12.7	30.9 $\pm$ 15.4	15.5 $\pm$ 12.9			27.1 $\pm$ 20.2	0.2–87.4
endurance	45.0 $\pm$ 61.4	46.7 $\pm$ 14.4	33.3 $\pm$ 13.4	20.7 $\pm$ 10.8			30.6 $\pm$ 18.6	1.6–88.4
lower body strength	41.6 $\pm$ 57.8	40.3 $\pm$ 14.1	27.1 $\pm$ 11.9	18.2 $\pm$ 8.7			26.1 $\pm$ 16.7	0.3–82.5
upper body strength	41.4 $\pm$ 56.6	46.9 $\pm$ 15.7	30.6 $\pm$ 14.1	16.1 $\pm$ 11.5			27.4 $\pm$ 19.6	0.5–81.4
upper body flexibility	57.7 $\pm$ 42.7	54.6 $\pm$ 13.6	49.7 $\pm$ 20.0	41.8 $\pm$ 18.6			47.4 $\pm$ 19.6	10.9–87.9

Note. CS-PFP-10 = 10-item continuous-scale physical-functional performance test.

Table 4
Correlation of Echocardiographic Variables With CS-PFP-10 Domains

	Domain					
	Total CS-PFP-10	Balance and coordination	Endurance	Lower body strength	Upper body strength	Upper body flexibility
LAVI (32)	-.59 <i>p</i> = .0005*	-.47 <i>p</i> = .009	-.63 <i>p</i> = .0002*	-.44 <i>p</i> = .01	-.45 <i>p</i> = .01	-.45 <i>p</i> = .01
PVAR (29)	.44 <i>p</i> = .02	.36 <i>p</i> = .06	.48 <i>p</i> = .01	.40 <i>p</i> = .04	.36 <i>p</i> = .06	.32 <i>p</i> = .11

Note. CS-PFP-10 = 10-item continuous-scale physical-functional performance test; LAVI = left atrial volume index; PVAR = pulmonary venous atrial reversal wave velocity. Values are Spearman correlation coefficients (rho) adjusted for age and gender. Numbers in parentheses are *n* values.

* Statistically significant correlation after Bonferroni correction for multiple comparisons (*p* < .001).