Effect of Echocardiographic Grading of Left Ventricular Diastolic Dysfunction by Different Classifications in Primary Care

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The presence of left ventricular (LV) diastolic dysfunction (DD) as characterized by Doppler echocardiography is associated with worse overall mortality both in symptomatic and asymptomatic patients. However, available data on this topic come from referral centers and have been obtained by different, validated algorithms for each single study. Thus, we aimed at determining the feasibility of comprehensive evaluation of LVDD in a primary care outpatient setting and at testing the concordance of different methodological approaches in grading diastolic dysfunction. Eight hundred eighty-five consecutive outpatients, in sinus rhythm, prospectively underwent Doppler echocardiography according to a predetermined protocol. Feasibility of each LV diastolic index and concordance between 3 methods to determine the degree of LVDD, namely the American Society of Echocardiography/European Association of Echocardiography (ASE/EAE) recommendations, the Olmstead County, and the Canberra Study protocols, were tested. Feasibility of all diastolic indexes was high, ranging from 93% of Valsalva maneuver to ≥99% for mitral inflow and tissue Doppler parameters. Diastolic function was not classifiable in 6% to 19% of patients. The concordance for LV diastolic dysfunction degree was fair when comparing the classification of the ASE/EAE with those from Olmstead County ($\kappa = 0.25$; reclassification rate 51%) and Canberra Study ($\kappa = 0.27$; reclassification rate 43.7%), and was good for the comparison between the Olmstead County and Canberra classifications ($\kappa = 0.68$, reclassification rate 27%). In conclusion, feasibility of LV diastolic function measurements is very high and grading diastolic dysfunction is possible in most patients in primary care settings. Substantial differences, however, exist when concordance is tested among 3 documented criteria, resulting in poor concordance of data interpretation and hence patient stratification and clinical management. **(Am J Cardiol 2015;116:1144−1152)**

Comprehensive evaluation of left ventricular (LV) diastolic dysfunction (DD) is a clinically relevant component of echocardiographic examinations because it assists in symptom interpretation and in predicting prognosis in patients with various cardiac syndromes.[1−7] The overtime use of diastolic parameters identifies patients who develop signs of function instability and who need urgent intervention to avoid potentially preventable death. A typical scenario is heart failure with Doppler signs of raised filling pressures which is known to limit patient's exercise capacity and provoke LV arrhythmias. Even in the setting of heart failure with preserved ejection fraction, diastolic measurements play a pivotal role in explaining symptoms and predicting prognosis.[7,8] Available cut-off values for grading DD are based on individual guidelines, which all originate from renowned international centers with years of expertise in the field. However, various documented studies have different grading algorithms which might make their direct application in daily cardiology outpatient services of limited clinical value.[1,9,10] To test this hypothesis, we performed a comprehensive evaluation of LV diastolic function in a consecutive group of outpatients referred by general practitioners to primary care echocardiographic laboratories, to explore the feasibility of DD assessment in a noncardiac center setting and to test the concordance of different methodologic approaches in grading DD.

Methods

For the purpose of the GRAding Diastolic dysfunction in Outpatients (GRADO) Study, 885 consecutive outpatients aged >14 years, referred to primary care laboratories for an echocardiographic examination, were prospectively enrolled. Exclusion criteria were sinus tachycardia (>100

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See page 1151 for disclosure information.

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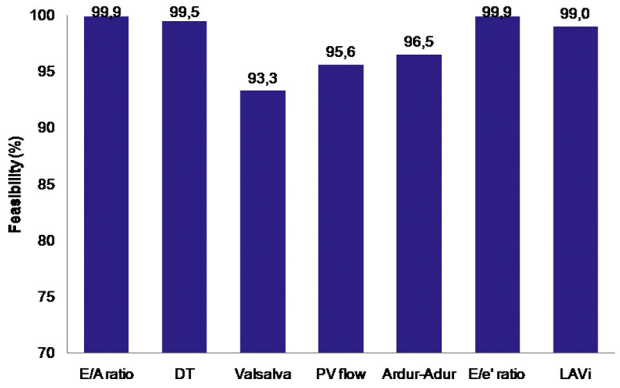

Figure 1. Feasibility of all the measurements used to assess left ventricular diastolic function. Percentages of patients in whom each parameter of LV diastolic function was measurable.

duration (A_{dur}) were measured at baseline and during the strain phase of the Valsalva maneuver, to reduce LV preload and elicit changes in LV inflow to distinguish normal from pseudonormal patterns.[1] A decrease of 20 cm/s in peak E velocity was considered adequate in patients with reversible restrictive filling pattern, and a relative decrease of ≥50% or an absolute decrease of ≥0.5 in the E/A ratio, based on each classification, a highly specific feature of increased LV filling pressures.[1,13] Pulmonary vein peak systolic (S) and diastolic (D) flow velocities, S/D ratio, and atrial reversal flow (AR) velocity were recorded and the duration of flow at atrial contraction (AR_{dur}). The difference between AR_{dur} and A_{dur} were calculated, with an $AR_{dur} - A_{dur} > 30$ ms as an early and reliable marker of increased LV end-diastolic pressure, independent from ejection fraction. Mitral annular velocities (septal and lateral) were measured by

Table 1
Distribution of the main parameters of diastolic function according to different cut-off values for each convention

	E/A	DT (ms)	E/e'
ASE/EAE	<0.8: n=217(24.5%) 0.8-1.5: n=544 (61.5%) >1.5: n=124 (14.0%)	>200: n=451 (51.2%) 160-200: n=288 (32.7%) <160: n=142 (16.1%)	Average <8: n=523 (59.3%) 9-12: n=309 (35.0%) >13: n=50 (5.7%)
Olmstead County	<0.75: n=156 (17.6%) 0.75-1.5: n=605 (68.4%)	>140: n= 830 (94.2%)	Septal ≥10: n=261 (29.6%)
Canberra Study	>1.5: n=124 (14.0%)	>160: n= 739 (83.9%)	Lateral ≥10: n=127 (14.4%)

Values are n (%).

E/A = peak early to late mitral diastolic velocities ratio; E/e' = peak early mitral diastolic velocity to peak early annular diastolic velocity ratio; DT = mitral E wave deceleration time.

beats/min), atrial fibrillation or flutter, either complex or frequent (i.e., 0.10 ectopic beats/h on Holter monitoring) supraventricular or ventricular arrhythmias, mitral stenosis, any other valvular disease of more than mild severity, severe mitral annulus calcification, previous mitral valvuloplasty, valve prosthesis, permanent pacemaker stimulation, complete right or left bundle branch block, and inadequate acoustic windows. All patients underwent a targeted history, standard 12-lead electrocardiogram, and comprehensive Doppler echocardiography. Body surface area, body mass index (BMI), systolic and diastolic blood pressure, and heart rate were calculated using conventional procedures. Informed consent was obtained from each patient, and the study protocol conformed with the ethics guidelines of the 1975 Declaration of Helsinki according to a priori approval by the institution's human research committee. Studies were prospectively performed by 3 independent, board-certified cardiologist, with >15 years of clinical experience in performing and interpreting echocardiographic examinations, using commercially available ultrasound systems, according to a predetermined protocol.[11] LV size and function were assessed according to the American Society of Echocardiography/European Association of Echocardiography (ASE/EAE) recommendations.[12] All the indexes for assessing diastolic function were measured from the apical views. Mitral inflow peak early (E) and late diastolic (A) velocities, E/A ratio, E wave deceleration time (DT), and A wave pulsed-wave tissue Doppler imaging.[1] Peak systolic (s'), early diastolic (e'), and late diastolic (a') velocities were measured at the 2 annular sites and averaged. The septal, lateral, and average E/e' ratios were calculated.[14–16] Mitral annular velocities are used to draw inferences about LV relaxation and E/e' can provide an estimate of LV filling pressures.[1] Left atrial volume was obtained from dedicated views and indexed to body surface area (LAVi).[17] All examinations were performed after fine adjustment of both ultrasound and pulsed Doppler beam orientation and sample volume positioning, after careful optimization of spectral gain and filter settings, taking the average of 3 consecutive beats for each measurement.

Three different classifications of LV diastolic dysfunction (DD) were considered and compared in this study. The first was that of the joined ASE/EAE recommendations for the evaluation of LV diastolic function by echocardiography.[1] This classification suggests a practical scheme for grading DD starting from both septal and lateral e' and LAVi. For abnormal values of LAVi and e', it recommends a comprehensive evaluation based on the use of specific cut-off values for E/A and DT, of the results of the Valsalva maneuver, of average E/e', and of $AR_{dur} - A_{dur}$, finally identifying 3 grades of LVDD. The second classification has been validated in residents aged ≥45 years of Olmsted County, Minnesota,[9] and identifies 4 categories of LV diastolic function, namely normal function, mild, moderate,