Noninvasive Estimation of Left Ventricular Compliance Using Three-Dimensional Echocardiography

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Background: Left ventricular (LV) compliance is an important determinant of LV function and can be affected by a variety of cardiovascular conditions. In particular, diastolic dysfunction is associated with altered LV compliance. However, the evaluation of LV compliance is complex. Although the end-diastolic pressure-volume relationship (EDPVR) allows a direct, accurate evaluation of LV compliance, it requires invasive measurements. The aim of this study was to test the feasibility of noninvasive estimation of the EDPVR as a tool to evaluate LV compliance using three-dimensional echocardiography.

Methods: Sixty-eight subjects were studied, including 23 normal controls, 22 patients with increased LV compliance due to dilated cardiomyopathy, and 23 patients with reduced LV compliance secondary to isolated diastolic dysfunction as defined using current American Society of Echocardiography guidelines. The EDPVR was calculated for each subject using a nonlinear model with echocardiographic estimates of end-diastolic pressure and volume. For both the isolated diastolic dysfunction and dilated cardiomyopathy groups, predicted end-diastolic volumes at predetermined pressure values (5, 10, 20, and 30 mm Hg) were compared with values in normal controls.

Results: Compared with controls, noninvasive estimates of the EDPVR resulted in predicted end-diastolic volumes that were lower in the isolated diastolic dysfunction group and higher in the dilated cardiomyopathy group ($P < .0001$ for all four pressure levels). In addition, a stepwise trend of decreased compliance was noted for the different grades of diastolic dysfunction.

Conclusions: This is the first study to demonstrate the feasibility of noninvasive estimation of the LV EDPVR and its ability to differentiate normal from abnormal LV compliance using three-dimensional echocardiography.
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Keywords: Pressure-volume loop, Ventricular compliance, Diastolic function, End-diastolic pressure-volume relationship, Three-dimensional echocardiography

It is widely accepted that left ventricular (LV) diastolic dysfunction is an important independent clinical entity and a strong determinant of outcomes in a variety of cardiovascular conditions.[1-4] However, its evaluation is complex and remains difficult because of the lack of an established gold standard. Although LV pressure-volume loops can provide information about intrinsic LV compliance, via analysis of the end-diastolic pressure-volume relationship (EDPVR),[5,6] this methodology relies on invasive measurements and manipulations of loading conditions[7,8] and consequently is not used in clinical practice. Instead, clinical evaluation of LV diastolic function is performed noninvasively, mostly using Doppler echocardiography. The current approach recommended by the American Society of Echocardiography (ASE) consists mostly of the interpretation of atrial volume, mitral flow, and mitral annular velocity measurements using multiple criteria.[1] This approach is at times difficult to apply and may lead to ambiguous results.[9] Accordingly, additional tools to assess LV diastolic function are needed to address this issue.

Recently, a theoretical framework was developed to estimate the EDPVR without the need to manipulate loading conditions,[10] thus considerably simplifying this approach. Although to date, this methodology has been tested mainly with invasive pressure and volume measurements,[11] it could potentially become fully noninvasive, as recently suggested by Lam *et al.*,[12] using two-dimensional echocardiography. Accordingly, the aim of this study was to assess an alternative tool to noninvasively evaluate LV compliance by estimating the EDPVR using three-dimensional (3D) and Doppler echocardiography. To achieve this goal, we conducted a study in which noninvasive estimates of the EDPVR were compared between normal subjects and two groups of patients with increased and decreased LV compliance.

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Abbreviations

ASE = American Society of Echocardiography

DCM = Dilated cardiomyopathy

DT = Deceleration time

dtPVFd = Pulmonary venous flow diastolic deceleration time

EDP = End-diastolic pressure

EDPVR = End-diastolic pressure-volume relationship

EDV = End-diastolic volume

IDD = Isolated diastolic dysfunction

LAVi = Left atrial volume indexed to body surface area

LV = Left ventricular

3D = Three-dimensional

METHODS

Participants

After the exclusion of eight subjects with inadequate echocardiographic images, we studied a total of 68 subjects who were ≥18 years of age. The normal control group consisted of 23 subjects with LV end-diastolic volumes (EDVs) < 140 mL, ejection fractions > 55%, and no diastolic dysfunction using current ASE guidelines.[1] The reduced LV compliance group included 23 patients with isolated diastolic dysfunction (IDD), which was defined as diastolic dysfunction according to ASE guidelines with normal LV EDV (<140 mL) and ejection fraction (>55%). All patients in this group had variable degrees of LV hypertrophy secondary to systemic hypertension: 17 mild, four moderate, and two severe. In addition, an increased LV compliance group was studied, consisting of 22 patients with dilated cardiomyopathy (DCM). Patients with more than mild mitral regurgitation were excluded. Study subjects' characteristics are presented in Table 1. Patients in both groups received individualized standard-of-care treatment, and no therapy was withheld for the purposes of this study. The protocol was approved by the institutional review board, and each subject provided informed consent.

Echocardiographic Data Acquisition and Analysis

Echocardiographic imaging was performed using an iE33 ultrasound system (Philips Medical Systems, Andover, MA). Two-dimensional and Doppler imaging was performed using an S3 transducer. Apical four-chamber views were acquired, and standard single-plane calculation was used to obtain maximal left atrial volume, which was indexed to body surface area (LAVi). Pulsed Doppler was used in the apical four-chamber view to obtain early (E) and atrial (A) peak mitral flow velocities, as well as the deceleration time (DT) of the early mitral flow. In addition, tissue Doppler was used to obtain septal (e'_{sept}) and lateral (e'_{lat}) mitral annular early peak velocities, as well as their average (e'_{avg}). From these measurements, the E/A and E/e'_{avg} ratios were calculated.

Pulmonary venous flow, used to measure diastolic DT (dtPVFd), was acquired from the apical four-chamber view by positioning the pulsed-wave Doppler sample volume in the right upper pulmonary vein (Figure 1). Thereafter, LV end-diastolic pressure (EDP) was determined using two different equations previously described by Lam *et al.*[12] (EDP = 11.96 + 0.596 × E/e′) and Olariu *et al.*[13] (EDP = 36.7651 − 0.10299 × dtPVFd).

Real-time 3D echocardiographic imaging was performed using an X5 transducer in wide-angle "full-volume" acquisition mode, in which four wedge-shaped subvolumes were obtained over consecutive cardiac cycles during a single breath hold. Special care was taken to include the entire LV cavity within the pyramidal scan volume. After gain settings were optimized for endocardial visualization, three to four data sets were acquired and stored digitally for offline analysis. Then, 3D images were analyzed offline using commercial software (3DQ QLAB; Philips Medical Systems). Initially, two-chamber and four-chamber views with the largest long-axis dimensions were selected from the pyramidal data set in the first time frame of the data set (i.e., end-diastole), as described previously.[14] In these two planes, five points—four points on the mitral annulus (two in each plane) and the apex in either plane—were manually initialized to define the endocardial surface. Then, the endocardial surface was manually adjusted in multiple apical planes, while including the papillary muscles in the LV cavity, and its position was corrected as necessary in multiple arbitrary cut planes until the best match was visually verified, to obtain LV EDV. This process was then repeated for the frame depicting the smallest LV dimensions, resulting in LV end-systolic volume. Stroke volume was then calculated as EDV − end-systolic volume and ejection fraction as stroke volume/EDV.

Estimation of the EDPVR

On the basis of the assumption that EDPVR can be described by a nonlinear analytical expression as (Figure 2)

$$\text{LV EDP} = \alpha \times (\text{LV EDV})^{\beta}, \tag{1}$$

because of the nature of this relationship between LV pressure and volume, β mostly affects the shape of the EDPVR curve in the high-volume range, while α has more influence in the low-volume range.

Klotz *et al.*[10] initially developed a single-beat estimation technique for the EDPVR. They showed that given $V_0 = \text{LV EDV} \times (0.6 - 0.0006 \times$

Table 1 Study subjects' characteristics

Variable	Control (*n* = 23)	IDD (*n* = 23)	DCM (*n* = 22)	*P**
Age (y)	40 (33–46)	57 (44–76)	54 (42–68)	.0022
Men	16 (69%)	10 (44%)	18 (82%)	.022
Body surface area (m^2)	1.9 (1.7–1.9)	1.8 (1.7–1.9)	2.0 (1.8–2.0)	.07
LV ejection fraction (%)	61 (59–65)	63 (57–69)	31 (25–36)	<.0001
LV EDV (mL)	118 (104–139)	80 (68–102)	232 (203–258)	<.0001
LV ESV (mL)	44 (38–54)	34 (21–40)	163 (134–178)	<.0001
LV EDP (mm Hg) (Lam *et al.*[12])	15 (15–16)	20 (17–25)	20 (19–23)	<.0001
LV EDP (mm Hg) (Olariu *et al.*[13])	19 (17–20)	21 (18–23)	21 (19–24)	.045

Continuous variables are presented as median (interquartile range) and categorical variables as count (percentage).
*Kruskal-Wallis test.