Left atrial conduit volume is generated by deviation from the constant-volume state of the left heart: a combined MRI-echocardiographic study

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Submitted 13 October 2003; accepted in final form 26 January 2004

Bowman, Andrew W., and Sándor J. Kovács. The left atrial conduit volume is generated by deviation from the constant-volume state of the left heart: a combined MRI-echocardiographic study. Am J Physiol Heart Circ Physiol 286: H2416–H2424, 2004. First published January 29, 2004; 10.1152/ajpheart.00969.2003.—Although modeling the four-chambered heart as a constant-volume pump successfully predicts causal physiological relationships between cardiac indexes previously deemed unrelated, the real four-chambered heart slightly deviates from the constant-volume state by ventricular end systole. This deviation has consequences that affect chamber function, specifically, left atrial (LA) function. LA attributes have been characterized as booster pump, reservoir, and conduit functions, yet characterization of their temporal occurrence or their causal relationship to global heart function has been lacking. We investigated LA function in the context of the constant-volume attribute of the left heart in 10 normal subjects using cardiac magnetic resonance imaging (MRI) and contemporaneous Doppler echocardiography synchronized via ECG. Left ventricular (LV) and LA volumes as a function of time were determined via MRI. Transmirtal flow, pulmonary vein (PV) flow, and lateral mitral annular velocity were recorded via echocardiography. The relationship between the MRI-determined diastolic LA conduit-volume (LACV) filling rate and systolic LA filling rate correlate well with the relationship between the echocardiographically determined average flow rate during the early portion of the PV D wave and the average flow rate during the PV S wave ($r = 0.76$). We conclude that the end-systolic deviation from constant volume for the left heart requires the generation of the LACV during diastole. Because early rapid filling of the left ventricle is the driving force for LACV generation while the left atrium remains passive, it may be more appropriate to consider LACV to be a property of ventricular diastolic rather than atrial function.

Cardiac magnetic resonance imaging; Doppler echocardiography; left ventricular function; left atrial conduit volume

ONE OF THE ASSUMED PHYSIOLOGICAL features of cardiac function is the constant-volume attribute of the four-chambered heart, which states that the total volume of the four-chambered heart (i.e., the contents of the pericardial sack) remains invariant throughout the cardiac cycle (1, 8, 11, 12). The constant-volume attribute has immediate and direct consequences regarding cardiac function, particularly during diastole (1, 3, 18–20). The kinematic essence of the constant-volume attribute is that as the ventricles empty, the atria fill, which results in a simultaneous reciprocal of volumes. However, previous studies (1, 1a, 12) demonstrated that the four-chambered heart deviates slightly (by 5–8%) from the constant-volume state, and the maximum deviation consistently occurs at ventricular end systole and is corrected during early diastole.

The four-chambered heart were a perfect constant-volume pump, inflow into the heart [through the pulmonary veins (PVs) or vena cava] would be allowed only while there is simultaneous outflow (from the aorta and pulmonary artery). Consequently, the idealized constant-volume state requires that if there is no outflow from the pericardial sack, there can be no inflow. Therefore, for the constant-volume state to be strictly maintained, there can be inflow into the heart only during systole. For the left heart, the existence of the systolic PV S wave is in accordance with the constant-volume criterion of reciprocation of atrial and ventricular volumes; however, contrary to idealized constant-volume requirements, PV inflow also occurs when there is no ventricular outflow in the form of the diastolic PV D wave.

Because the constant-volume attribute of the heart dictates that atrial and ventricular volumes reciprocate throughout the cardiac cycle, the constant-volume state and deviations from it have consequences on atrial function as well. The function of the atria, particularly the left atrium (LA), has been well characterized and applied to disease states (5, 7, 10, 15, 21, 23, 26, 27, 29). The LA functions as a booster pump, reservoir, and conduit. However, the conduit function of the LA, originally defined as “the integrated net flow through the atrium . . . assigned neither to the reservoir nor to the pump function” (10), remains incompletely understood and, like the PV D wave, appears contrary to idealized constant-volume requirements.

Therefore, we investigated the fate and time course of the 5% deviation in the heart from the constant-volume state during the early rapid filling phase of diastole, with particular emphasis on how the deviation relates to the PV D wave and the left atrial conduit volume (LACV). We evaluated LA function and the LACV using volume data acquired via cardiac magnetic resonance imaging (MRI) and contemporaneous flow data acquired via Doppler echocardiography.

METHODS

Cardiac MRI. After appropriate informed consent was obtained according to Washington University Medical Center Human Studies Committee guidelines, 10 normal subjects (5 male) underwent a complete cardiac MRI and concurrent Doppler echocardiography.

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functional study. The MRI portion of our study has been previously described (1). Briefly, for the MRI study, the subjects were scanned with a 1.5-T Philips Gyroscan MRI system (release 9.0; Philips Medical Systems; Best, The Netherlands). Survey images and standard planes for four-chamber and short-axis views were obtained. Once determined, high-resolution cine loops of the four-chamber view were obtained during subject breathholds (duration, ~10 s each). These cine loops were divided into 20–27 cardiac phases triggered from the ECG R wave and covered the entire cardiac cycle.

The initial four-chamber view was used to plan a short-axis cine-stack protocol of 18–20 slices (9 mm thick with zero gap) spanning the apex of the ventricles through the superior-posterior wall of the left atrium. Image slices were obtained during 10-s breathholds per slice, and each cine loop was divided into 20 cardiac phases triggered from the ECG R wave and covered the entire cardiac cycle. For the short-axis stack image acquisition, the repetition time, echo time, and flip angle were 4.0 ms, 1.47 ms, and 50°, respectively. In-plane resolution of 1.41 mm was obtained with a field of view of 36 cm and a matrix size of 192 × 256 interpolated to 256 × 256.

Upon completion of the exam, the data were archived to 4.1-Gb magneto-optical disks. All image analysis was performed offline on a remote personal computer using eFilm 1.5.3 (eFilm Medical; Toronto, Ontario), Paint Shop Pro 7 (Jasc Software; Minnetonka, MN), and Scion Image (Scion; Frederick, MD).

In all subjects, the left ventricular (LV) and LA endocardial contours were manually traced in each slice at each phase of the three-dimensional dataset (Fig. 1), and the corresponding segmental volumes were determined. For each phase, the segmental volumes of the traces were summed via Simpson’s rule and compared over the cardiac cycle. The LA appendage was included in the measurement of LA volume. Intraobserver variability was determined using 10 randomly selected short-axis images of the LV and LA.

**Doppler echocardiography.** Either immediately before or after the cardiac MRI exam, while in the MRI laboratory, clinical echocardiographic images were obtained from all subjects in the left lateral decubitus position by an experienced sonographer [American Society of Echocardiography (ASE) certified] using an Acuson Sequoia (Acuson; Mountain View, CA) echocardiographic imaging system equipped with a 3.5-MHz transducer. The imager recorded and displayed on the image the simultaneous limb lead II of the ECG. The sample volume for transmural Doppler imaging was placed at the mitral leaflet tips in the apical four-chamber view in accordance with ASE criteria (25). The sample volume for PV flow waves was placed 1 cm upstream in the right superior PV. Doppler tissue imaging (DTI) of the lateral side of the mitral annulus was obtained using the apical four-chamber view. To minimize artifacts due to misalignment between the imaging beam and the flow to the extent possible, E-wave, PV-wave, and E’-wave data were obtained by aligning the scan direction along the line of motion of flow or the annular motion. All echocardiographic data were stored digitally on magneto-optical disk for subsequent offline analysis using ViewPro (Freeland; Westfield, IN) and Paint Shop Pro. Baseline filters were set to their lowest settings.

**Data analysis.** For the analysis between the MRI and ECG data, the MRI-derived LV and LA volume curves were temporally aligned using the QRS peak as the fiducial marker with representative echocardiographic transmitial, PV, and Doppler tissue images for each subject. Although it was not technically possible to acquire all of the images simultaneously, care was taken to select representative echocardiographic images at a heart rate as close to the average heart rate from the MRI scan as possible. To highlight the simultaneous volume and flow events of particular interest, the beginning of the Doppler E wave, the peak of the E wave, and the end of the DTI E’ wave were selected for analysis.

In each subject, the peak velocity and velocity-time integral (VTI) for the PV S and D waves were measured for three heartbeats and averaged. Average Doppler flow rates (in cm/s) were determined by dividing the VTI of a wave of interest by its duration. For the MRI data, average volumetric flow rates (in ml/s) were determined by fitting the MRI-derived volume curves with straight lines; the slope of the fit line was taken as the average volumetric rate of change (dV/dt) over the time range of interest.

**LACV determination.** Traditionally, the LACV, along with the reservoir and booster pump volumes, is calculated using discrete data points taken along the LA and LV volume curves (Fig. 2; Refs. 16, 30). Specifically, the LA booster pump volume (LABPV) is the difference in LA volume before and after atrial systole (points D and A on Fig. 2). The LA reservoir volume (LARV) is the difference between maximum LA volume and the mid-diastolic local minimal atrial volume (points B and C on Fig. 2). The LACV has been defined as the difference between the LV stroke volume (LVSV) and the sum of the LA reservoir and booster pump volumes (16, 30)

\[
\text{LACV} = \text{LVSV} - (\text{LARV} + \text{LABPV})
\]

Because cardiac MRI provides suitable spatial and temporal resolution of both LV and LA volumes (2, 31), we define the LACV more precisely as a function of time.

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**Fig. 1.** Typical magnetic resonance (MRI imaging) in short-axis view. A: endocardial trace of left ventricle (LV). B: endocardial trace of left atrium (LA). See text for details.
LACV(t) = [LV(t) - LV_{\text{min}}] - [LA_{\text{max}} - LA(t)] \tag{2} 

where \(LV_{\text{min}}\) refers to minimal LV volume (at end systole), \(LA_{\text{max}}\) refers to maximum LA volume (near end systole), and \(t\) denotes the time-dependent nature of the volumes during the cardiac cycle.

RESULTS

Subject demographics are listed in Table 1. Intraobserver variability for volume tracings was 3.8%. Figure 3A shows the typical plot of LV and LA volumes and the sum of the two as a function of time for a selected subject. Consistent with previous reports by our group (1) and others (11), the sum of the left heart chamber volumes (\(LA + LV\) volumes) does not follow the constant-volume attribute of the four-chambered heart as closely as the entire pericardial sack. When normalized to left heart chamber volume at ventricular end diastole, the left heart chamber volume varies by \(\sim 30\%\) with the maximum deviation occurring at end systole (in 7 subjects) or within 80 ms of end systole (in 3 subjects).

Figure 3B shows the LACV as a function of time during diastole for the same patient whose data are presented in Fig. 3A, as well as the total left heart volume as a function of time. Note the similarity in the shapes of the curves during diastole.

Figure 4 presents MRI-derived volume data aligned with echocardiographically derived flow data using the peak of the ECG QRS complex (solid gray line). Other time points of interest during the cardiac cycle have been highlighted as well. The dotted gray line indicates that the onset of the E wave (Fig. 4C) occurs, as expected, when LA volume is near its maximum (Fig. 4B) and at the same time as the onset of the PV D wave (Fig. 4D) and Doppler tissue E’ wave (Fig. 4E). The solid black line indicates that the peak of the E wave (Fig. 4C) occurs after the majority (on average, \(\sim 60\%\)) of the early rapid-filling volume has entered the left ventricle (Fig. 4A).

The dotted black line demonstrates that the end of the Doppler tissue E’ wave (Fig. 4E) occurs just after the end of the LA early diastolic emptying phase (Fig. 4B), after the peak of the Doppler E wave (Fig. 4C), and at or very near the peak of the PV D wave (Fig. 4D).

From the temporal linkage obtained from Fig. 4, the precise LACV data points that occur during the duration of the acceleration portion of the PV D wave (i.e., the duration of the DTI

Table 1. Study population

<table>
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<tr>
<th>Demographic Data for All Subjects</th>
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<td>Age, yr</td>
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<td>Weight, kg</td>
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Values are means ± SD; \(n = 10\) human subjects.

Fig. 2. Typical plot of MRI-derived left atrial (LA) volume vs. time for one normal subject, with time = 0 ms corresponding to the peak of the ECG QRS complex. **Point A** refers to minimal atrial volume at ventricular end diastole, **point B** indicates maximal atrial volume, **point C** refers to mid-diastolic relative minimal volume, and **point D** shows atrial diastolic volume immediately before atrial systole. ECG displayed is a schematic and serves as an aid to clarify timing within the cardiac cycle. See text for details.

Fig. 3. Left heart volumes. A: plot of left ventricular (LV) and LA volumes and the total left heart (LV + LA) volume as a function of time for one representative subject. B: total left heart (LV + LA) volume and the diastolic LA conduit volume (LACV) as a function of time for one representative subject. Note similarity of shape between the LACV curve and the diastolic portion of the left heart-volume curve. ECG displayed is a schematic and serves as an aid to clarify timing of the cardiac cycle. See text for details.
E' wave) were determined (data points between the dotted gray and black lines, see Fig. 5A). For all subjects, these data points were fit by linear regression to yield a slope or average rate of LACV filling (LACV_\text{fill}, in ml/s) during early diastole.

Similarly, using the LA volume curve, the data points between minimum and maximum LA volume (between points A and B in Fig. 2, during ventricular systole) were fit with linear regression to yield an average rate of LA filling (LA_\text{fill}, in ml/s) during ventricular systole (see Fig. 5B).

Using PV Doppler echocardiography, the average rate of LA filling during systole was determined as follows (see Fig. 6): for three representative beats, the VTI (in cm) divided by the duration (in s) yielded an average S value (S_{avg}, in cm/s) for each beat. S_{avg} was averaged for the three beats. In a similar manner using the same beats, the average value of the PV D wave (in cm/s) was determined between the D-wave onset and peak (D-pk_{avg}) and for the entire duration of the D wave (D_{avg}). Other selected parameters measured from PV images are listed in Table 2.

Fig. 4. “Synchronized” MRI-derived chamber volumes and echocardiographically derived flows from one representative normal subject. A: LV volume. B: LA volume. C: transmitial flow. D: pulmonary vein (PV) flow. E: lateral mitral annular velocity. Temporal points of interest include the peak of the QRS complex (solid gray line), the beginning of the Doppler E wave (dotted gray line), the peak of the E wave (solid black line), and the end of the Doppler tissue E’ wave (dotted black line). See text for details. E and A, transmitral E and A waves, respectively; S and D, PV S and D waves, respectively; E’ and A’, Doppler tissue E’ and A’ waves, respectively.

Fig. 5. Synchronized MRI-derived filling indexes and echocardiographic PV flow in a representative subject. A: diastolic LACV. Data points (in black) between the onset and peak of the PV D wave (gray dotted and black dotted lines, respectively) are fit using linear regression. In this example, the slope of the fit line (LACV_{\text{fill}}) is 197 ml/s. B: LA volume. Data points (in black) between the QRS complex and maximum LA volume (solid gray and black lines, respectively) are fit using linear regression. In this example, the slope of the fit line (LA_{\text{fill}}) is 128 ml/s. C: temporally aligned PV Doppler echocardiographic image. Solid gray, dotted gray, and dotted black lines represent the same events as in Fig. 4 (QRS complex, E wave beginning, and E’ wave end, respectively). Solid black line represents maximum LA volume. See text for details.
Echocardiographic flow velocity data cannot be directly related to MRI-derived volumetric data, because the size of the effective flow area (for example, the mitral valve area or PV orifice area) is unknown. Therefore, to compare the same physiological events in the cardiac cycle using the two methods, we normalized the data relative to the image method used. Consequently, we predicted that the ratio of LACVfl vs. LAfl (determined via MRI) should correlate with the ratio of D-pkavg to Savg (determined via PV echocardiography). The plot of LACVfl/LAfl vs. D-pkavg/Savg is shown in Fig. 7. The computed regression equation is LACVfl/LAfl = 0.95 × (D-pkavg/Savg) + 0.22; r = 0.76. We note that the numerical value of the slope for the linear regression is close to unity. Consequently, we predicted that the ratio of LACVfl vs. LAfl is shown in Fig. 7. The computed regression equation is LACVfl/LAfl = 0.95 × (D-pkavg/Savg) + 0.22; r = 0.76. See text for details.

**Table 2. Selected Doppler PV parameters**

| Peak S velocity, cm/s | 46±9 |
| Peak D velocity, cm/s | 58±8 |
| (Peak S)/(Peak D) | 0.79±0.16 |
| S-wave VTI, cm | 12.0±2.7 |
| D-wave VTI, cm | 13.5±3.2 |
| (S-VTI)/(D-VTI) | 0.94±0.31 |

Values are means ± SD; n = 10 human subjects. Peak, maximum velocity of S or D wave; VTI, velocity-time integral.

**Fig. 6.** Calculation of average flow rates in PV Doppler images. A: contour tracing of PV S wave (gray) and acceleration portion of D wave (black) to calculate velocity-time integrals. T S and T D-pk, duration times of the S wave and the acceleration portion of the D wave, respectively. B: mean flow value of S wave (Savg) and acceleration portion of D wave (D-pkavg) are displayed. In this example, Savg = 29 cm/s and D-pkavg = 44 cm/s. See text for details.

**Fig. 7.** LACVfl/LAfl vs. D-pkavg/Savg relation is shown for all 10 subjects. Dashed line indicates linear regression-determined best fit. Computed regression equation is LACVfl/LAfl = 0.95 × (D-pkavg/Savg) + 0.22; r = 0.76. See text for details.

**DISCUSSION**

We measured cardiac MRI-derived volume curves of the left ventricle and LA and used them to derive an expression of the LACV as a function of time. Not surprisingly, the shape of the LACV during diastole mirrors that of the sum of the LA and LV volumes. Closer inspection of Eq. 2 reveals that it may be rewritten as

\[
LACV(t) = (LV(t) + LA(t)) - (LV_{\text{min}} + LA_{\text{max}})
\]

which predicts that the LACV curve is identical to the left heart (LA + LV) volume curve except for a constant offset (LV_{\text{min}} + LA_{\text{max}}). Differentiating both sides of Eq. 2 (or Eq. 3) with respect to time predicts that the rate of change of the total left heart volume must be equal to the rate of change of the LACV during diastole.

Applying Eq. 2 (and/or Eq. 3) to the entire cardiac cycle illustrates that the LACV itself is defined by the change in total left heart volume during systole (see Fig. 8). Additionally, Eq. 3 demonstrates that the left heart will be a perfect constant-volume system if and only if LACV = 0 for all times \( t \). Therefore, the deviation of the left heart from the idealized constant-volume state demands the existence of a conduit volume, and conversely, the existence of the LACV requires that the left heart fail to obey the ideal constant-volume pump constraint.

Our methods allow us to relate Doppler transmitral flow, PV flow, Doppler tissue mitral annulus velocity, and MRI-derived LV and LA volume curves to one another (see Fig. 4) to evaluate LV and LA function. The alignment of the data in this fashion yields new insights into left heart function. For example, the echocardiographic PV flow profile indicates that the LA fills during both systole and diastole via the S and D waves (see Fig. 4D; Ref. 22). However, consideration of the MRI-generated LA volume curve (see Fig. 4B) linked to the PV flow profile (see Fig. 4D) demonstrates that the LA actually fills only during systole via the S wave. Although there is inflow from the PVs veins into the LA during early diastole (the D wave), LA volume is not increasing but actually decreasing...
changes in apparent size of Doppler flow profiles. For example, end-diastolic total left heart volume correlates weakly with the PV D wave VTI ($r = 0.41$; data not shown); however, LACV$_{fill}$, which is a volumetric flow measurement, correlates well with end-diastolic total left heart volume ($r = 0.91$; data not shown). Dividing LACV$_{fill}$ and D-pk$_{avg}$ by LA$_{fill}$ and S$_{avg}$, respectively, effectively accounts for the effect of heart size (and orifice area), allowing for the relationship between LACV filling and the PV D wave to be more discernible.

It is interesting to note that, although the E wave lasts longer than the E’ wave, only a small amount of (MRI-determined) volumetric flow enters the left ventricle after the end of the E’ wave, that is, after the cessation of long-axis expansion of the left ventricle (see Fig. 4A). Although the effective mitral valve area is frequently modeled as a constant (3, 18–20), in reality, it is time varying. The mitral valve leaflets behave as a windsock: the faster that blood flows through the valve, the more the leaflets separate and the greater the effective mitral valve area. At slower flow velocities (near the end of the E wave), the effective mitral valve area should be smaller than during earlier, higher flow velocities. This time- and flow-dependent change in effective valve area can explain the mechanism by which the LV volume increases the most rapidly during the acceleration portion of the E wave ($\sim 60\%$ of the E-wave volume enters the left ventricle by the peak of the E wave; see Fig. 4, A and C). Studies designed to further elucidate the changes in effective mitral valve area during the course of diastole are in progress.

Subsequent examination of Fig. 4 also suggests that the orifices of the PVs change in size during the cardiac cycle as well. The results illustrate that the majority of the LACV enters the left ventricle during the acceleration portion of the PV D wave (see Figs. 4 and 5). However, because the peak of the D wave (see Fig. 4D) is virtually simultaneous with the end of both the DTI E’ wave (see Fig. 4E) and early diastolic volumetric LV filling (see Fig. 4A), the deceleration portion of the D wave primarily appears to only minimally fill the LA during the mid-diastolic expansion phase. There is a large discrepancy between the magnitude of the LACV and the volume of LA mid-diastolic expansion but little difference between the VTI of the acceleration and deceleration portions of the D wave. This discrepancy may be resolved if, like the mitral valve area, the effective area of the PVs is time varying throughout diastole as well. However, unlike the mitral valve area, the PV area may not be larger at higher flow rates. Instead, PV areas are likely the largest when the left atrium itself is the largest and the most distended, that is, near ventricular end systole. A larger PV area at the beginning of diastole would facilitate the rapid filling of the left ventricle via the LACV mechanism as the data suggest. Conversely, a smaller PV area during atrial contraction would help to limit the retrograde flow into the PVs and assist LV filling at the end of diastole. Recent studies (9) show that atrial myocardium extends into the orifice of the PVs for nearly a centimeter and the myocardial fibers are circumferentially oriented. Such atrial myocardium, when contracting, would constrict the PV orifice like a sphincter and aid in directing blood from the LA to the left ventricle during atrial systole. Additional studies to address the time-varying nature of the PV inlet area are currently in progress.

These results should not be interpreted as showing that the LV filling volume that occurs before the peak of the D wave

Fig. 8. MRI-determined total left heart (LA + LV) volume and mathematically derived LACV from Eq. 3 as functions of time throughout the cardiac cycle. Identical shapes of both curves prove that deviation of total left heart volume from constant accounts for LACV. ECG displayed is a schematic and serves as an aid to clarify timing of the cardiac cycle. See text for details.
results only from the LACV. On the contrary, the data also clearly de-
noted as such in terms of LV

tions may be resolved with the realization that the three

tions defined in terms of LV function (LVSV, see Eq. 1;Refs. 10, 16, 30). This apparent misattribution or misperception may be resolved with the realization that the three “func-
tions” of the LA (booster pump, reservoir, and conduit) are actually defined as such in terms of LV filling (10, 23). That is, the left atrium acts as a booster pump to the left ventricle, a reservoir for the left ventricle, and a conduit into the left ventricle. The attributes of the left ventricle dictate these functions of the LA. Although the LA booster pump function (atrial systole) is most dependent on intrinsic atrial attributes, such as atrial contractility, it is highly modulated by ventricular properties (13, 23, 26, 27). During ventricular systole, the left ventricle pulls the mitral valve plane toward the ventricular apex and the aortic root anteriorly and thereby aspires blood (the LA reservoir blood) into the LA; analogous to the motion of the piston in a syringe (see the supplemental data animation at http://ajpheart.physiology.org/cgi/content/full/00969.2003/ DC1). LV contraction also decreases the overall volume of the left heart, which in effect stores elastic strain energy for diastolic filling. The amount by which LV systole reduces the total left heart volume will determine how much blood must flow through the LA during diastole directly into the left ventricle (the LACV). Because the LACV is effectively drawn into the left ventricle via LV suction while the LA is passive, it may be more appropriately viewed as a property of LV diastolic function rather than intrinsic LA function. 

Limitations. In this study, when evaluating the constant-volume attribute of the heart, we considered only the left heart, and specifically, only the LV and LA chamber volumes. Although we did not evaluate the right side of the heart directly, previous studies have concluded that the left and right hearts independently behave as constant-volume pumps (11), and our own previous results suggest that the right heart adheres to the constant-volume attribute better than the left heart (1). Within the pericardial sack, left heart structures also include portions of the aortic root. In our previous study, we noted that movement of the aortic valve plane toward the apex during systole causes the volume of the aortic root within the pericardial sack to actually increase, whereas during diastole it decreases. This effect attenuates the overall change in left heart volume during the cardiac cycle as depicted in Fig. 3. However, the sum of the LV and LA volumes substantially domi-
nates the overall left heart volume variation; hence, the small effect of aortic root volume variation in this study was ignored for the sake of simplicity. 

Because the MRI scan and echocardiographic study were contemporaneous but not simultaneous, we were unable to assure the maintenance of a constant heart rate in our subjects. Because the MRI imaging involved frequent breathholds, the measured heart rates of some subjects were found to be different during the MRI scan than during the echocardiographic study (from ~60 to 80 beats/min). However, during such minor changes in heart rate, the changes in duration of systole and diastolic early rapid filling appear minimal; the change in cardiac cycle duration is primarily accounted for by change in the duration of diastasis, when no significant flow occurs. Additionally, we note that the timing of events during systole and early diastole were consistent between the echo-
cardiographic and MRI measurements even when the heart rates of subjects varied somewhat between the two studies. However, we also note that the use of breathholding during the MRI exam and its absence during the echocardiographic exam may introduce some differences in the transmirtal pressure gradients present during the two studies. Because all the subjects were young, in good physical condition, and performed short (~10 s) breathholds, such differences in pressure gradients were likely minimal. 

Because the MRI volumetric data were acquired using 9-mm-thick slices, there is a possibility of systematic error in the volumes reported in this study. This error is most likely the largest when the chamber to be measured is the smallest and has the thinnest walls (i.e., the LA). However, the technique employed in this study is the current research standard: previous MRI studies evaluating atrial size have used a similar if not larger slice thickness (1, 16, 17, 24, 30). Manual tracings of the chambers may also raise concern, but it has also been the standard approach for chamber volume determination. A recently developed automated edge-detection method for volume measurement showed excellent agreement relative to the current gold standard that consists of manually traced segmental volumes (30).

Limitations of transthoracic PV echocardiographic imaging have been well characterized (22, 28). Frequently, only one vein may be imaged clearly. Previous studies using both echocardiography and MRI have demonstrated that flow through the four PVs can vary because different veins can exhibit different flow contours (4, 6). However, considering that the PV measurements used to calculate D-pkavg and Savg in this study were, at best, first-order approximations of net inflow rates into the left atrium, the strength of the measured relationship between LACVavg/LAavg and D-pkavg/Savg was substantial. 

It is evident from inspection of Eqs. 1 and 2 that the LACV derived from Eq. 2 at ventricular end diastole will not neces-
sarily have the same value as the LACV calculated using Eq. 1. The discrepancies between the two values relate to factors such as how much the LA volume increases during the mid-diastolic expansion phase and the amount of the LA stroke volume that fills the left ventricle instead of emptying back into the PVs. A benefit of using Eq. 2 instead of Eq. 1 to calculate LACV is that Eq. 2 is more consistent with the intuitive notion of a conduit volume passing directly from the PVs to the left ventricle. Regardless, the overall values are similar, if not, identical, between the two methods.
We also note that the data indicate that the MRI-determined LV volume begins to increase before the beginning of the Doppler E wave (see Fig. 4, A and C). The shape of the LV volume curve is similar in all subjects in this study and consistent with other published MRI-derived volume curves (30), all of which indicate a single data point of minimum LV volume, even in scans with sufficient temporal resolution to image multiple time points during isovolumic relaxation. This slight increase in volume before the onset of the E wave is likely an artifact of the MRI volume-measurement method. The rotational/torsional and slight geometric changes in the left ventricle during isovolumic relaxation may lead to the appearance of mildly increasing volume in the imaging plane employed in this study. The slice thickness of 9 mm may also mask small longitudinal motions of the mitral valve that serve to conserve LV volume during wall relaxation during the isovolumic period of diastole. Consistently, however, the data show that, at the onset of the Doppler E wave, the rate of LV filling (measured via MRI) increases dramatically, which reinforces our confidence in the accuracy of the temporally aligned data sets.

We conclude that, although the idealized constant-volume attribute of the four-chambered heart is useful for modeling intrapericardial dynamics, the deviation of the heart from the constant-volume state by 5% has intriguing and novel consequences due to conservation of mass. These consequences include the very existence of the PV D wave and the LACV, both of which violate the strict constant-volume attribute of the left heart. The variation in total left heart volume at end systole accurately predicts the nature of the LACV during diastole. The rate of LACV filling of the left ventricle during diastole, when scaled to the rate of LA filling during systole, accurately predicts the average rate of PV inflow during the acceleration portion of the D wave, similarly scaled to the average rate of PV inflow during the S wave. The temporal relationships between standard echocardiographic events and MRI-derived chamber volumes provide new insight into global left heart function during diastole and the time dependence of the effective mitral valve and PV areas. Additional studies involving LV volumes in conjunction with LA volumes in pathological states as well as studies involving the right heart are in progress.

ACKNOWLEDGMENTS

The authors thank Shelton Caruthers for technical direction, Mary Watkins and Todd Williams for MRI acquisition, Peggy Brown for expert echocardiographic image acquisition, and Tim Meyer for helpful comments regarding manuscript preparation.

GRANTS

This work was supported in part by the Heartland Affiliate of the American Heart Association (Dallas, TX), the Whitaker Foundation (Roslyn, VA), National Heart, Lung, and Blood Institute Grants HL-54179 and HL-04023 (Bethesda, MD), the Alan A. and Edith L. Wolff Charitable Trust (St. Louis, MO), and Philips Medical Systems (Best, The Netherlands).

REFERENCES