Evaluation of Left Atrial Function by the Functional Volume Change Curve Derived From Doppler Flow Spectra

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The objective of this study was to clarify the left atrial (LA) reservoir and booster pump function in patients with left ventricular (LV) diastolic dysfunction. To determine LA reservoir and booster pump function, a new algorithm to determine LA functional volume change curve (FVC) was developed from Doppler flow spectra of pulmonary venous flow and LV inflow by transthoracic echocardiography in 110 patients. Patients were classified into normal (N), and abnormal (AB) and pseudonormal (PN) groups on the basis of their Doppler flow patterns. From the indices of FVC, atrial reservoir volume (ARV), passive emptying volume (PEV) and active emptying volume (AEV) were obtained. ARV/stroke volume (SV) was increased in the AB group, but decreased in the PN group compared with N (N, 0.61 ± 0.09 ; AB, 0.73 ± 0.10 ; PN, 0.52 ± 0.13 , $p < 0.05$). PEV/SV was significantly decreased in AB, but increased in PN compared with N (N, 0.27 ± 0.07 ; AB, 0.19 ± 0.07 ; PN, 0.31 ± 0.18 , $p < 0.05$). AEV/SV was significantly increased in AB, but decreased in PN compared with N (N, 0.41 ± 0.08 ; AB, 0.56 ± 0.10 ; PN, 0.26 ± 0.19 , $p < 0.05$). Thus, in patients with an abnormal relaxation pattern, the LA reservoir and booster pump function are augmented, but in patients with a pseudonormal pattern, both LA reservoir and booster pump function are deteriorated, suggesting a vulnerability to pulmonary congestion. (*Jpn Circ J* 2001; 65: 953–957)

Key Words: Doppler echocardiography; Left atrial function; Left ventricular diastolic function; Volume curve

Left atrial (LA) function can be evaluated by measuring pressure and volume, constructing the pressure–volume relationship and the dimensional changes of the LA can replace LA volume.^{1–8} LA function has 3 components: reservoir, conduit and booster pump functions.^{5,6,9,10} The reservoir function indicates the storage capacity for pulmonary venous (PV) return by LA distension during ventricular systole. During ventricular diastole, the LA works as a conduit for blood flow from the PV to the left ventricle (LV). The booster pump function indicates the filling blood volume to the LV during atrial systole. Recently, it is shown that atrial natriuretic peptide (ANP) synthesis is activated by the stimulus of atrial stretch, and the booster pump function of LA is strongly related to the release of ANP.^{11,12} Therefore, it is important to estimate the LA function in detail to understand the hemodynamic status of patients with heart failure.

In spite of its importance, it is difficult to estimate LA function, particularly the 3 components of LA function, because of the difficulty in determining the change in LA volume correctly. Thus, we developed a new method for measuring the LA volume change independent of the LA shape using Doppler flow spectra. PV flow (PVF) velocity and LV inflow (LVIF) velocity were measured by Doppler echocardiography, and from these flow velocity data the

LA functional volume change curve (FVC) was constructed by a newly developed algorithm described in detail in the Methods section. Using the FVC, we evaluated LA reservoir and booster pump functions, respectively, in patients with normal and abnormal LV diastolic function.

Methods

Study Patients

The 110 consecutive patients (male 68, female 42) who did not have mitral regurgitation were enrolled in this study. The mean age of the population was 61.6 ± 12.5 years (range, 26–86). The following heart diseases were involved: coronary artery disease, 42; myocarditis, 11; hypertrophic cardiomyopathy, 4; dilated cardiomyopathy, 4; aortic regurgitation, 2; ventricular septal defect, 2; sick sinus syndrome, 1. Thirty-two patients had no heart disease, 4 had respiratory disease and 8 had undergone hemodialysis.

Transthoracic Echocardiography

Echocardiography was performed using ALOKA SSD-2200 with a 2.5MHz probe in the left lateral decubitus position during quiet respiration. The variability of the R-R interval never exceeded $\pm 5\%$.¹³ To record LVIF, the sample volume was placed at the mitral tip in the left anterior oblique-like view.^{14,15} For PVF, the color Doppler method was used to identify the PV orifice and the sample volume was placed at the right or left upper PV within 15mm of its orifice in either the 4- or 2-chamber view.^{15,16} Standard M- and B-mode echocardiography was recorded and % fractional shortening (%FS) and stroke volume (SV) were calculated from M-mode echocardiography.

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Fig 1. Schema of the composition of the left atrial functional volume change curve (FVC) derived from Doppler flow spectra. PVF, pulmonary venous flow; LVIF, left ventricular inflow; $dV(LA)/dt$, the first derivative of left atrial volume change; χ , constant.

Computation of FVC

Because the LVIF pattern is similar to the pattern of the first derivative of LV volume change during ventricular diastole, LV volume change can be predicted by LVIF.¹⁷ We applied this concept to the LA volume change during 1 cardiac cycle. Theoretically, the inflow volume to the LA and its outflow volume during 1 cardiac cycle are equal. Instantaneous differences between the inflow and outflow volumes indicate the first derivative of LA volume change ($dV(LA)/dt$). Thus, the algorithm to integrate the difference between LA inflow and outflow gives the FVC.

The schema of the computation of the FVC is shown in Fig 1. When we assume that the mitral annular and PV diameters are unchanged during 1 cardiac cycle and that the 4 PV flow patterns are similar, the following equation is obtained: mitral valve annular area $\times$ the velocity-time integral (VTI) during a cardiac cycle of LVIF = the sum of 4 PV cross-sectional areas $\times$ VTIs during a cardiac cycle of PVF.

With a constant χ = mitral valve annular area/the sum of 4 PV cross-sectional areas, the formula becomes as follows: VTI of LVIF = VTI of PVF.

The instantaneous difference between PVF and χ LVIF produces $dV(LA)/dt$. Then, we computed the integrals of $dV(LA)/dt$, which produces the FVC.

The VTI of PVF during ventricular systole (Sa) was measured from the onset of the forward flow to the onset of the diastolic flow, which was defined as the nadir between systolic and diastolic waves. The VTI of PVF during ventricular diastole (Da) was measured from the nadir between systolic and diastolic waves to the termination of the diastolic forward wave. The VTI of PVF during atrial systole (Aa) was measured from the onset up to the termination of the backward flow. Atrial reservoir volume (ARV), which was the difference between LA maximum and minimum volumes, was calculated with the following formula¹⁶: $ARV = SV \times Sa / (Sa + Da - Aa)$.

From the FVC, we calculated the passive emptying volume (PEV), which represents the decreased volume from the LA with LV early diastolic filling, and the active emptying volume (AEV), which represents the decreased volume from the LA by LA contraction (Fig 2). We evaluated LA function by ARV, PEV, AEV, and their values corrected by SV^{5,6,9,10,18}

NIH image V1.61 (Wayne Rasband, National Institutes of Health), image-processing software¹⁹ was used to obtain the FVC. We imported PVF and LVIF spectra during 1 cardiac cycle from the peak of the R wave on the ECG into

Fig 2. Left atrial functional volume change curve divided into 4 phases: (1) an active filling phase, (2) a passive emptying phase, (3) a diastasis, (4) an active emptying phase.

the computer. By NIH image loading the FVC calculation macro, the pixels of the 2 spectra were counted and the FVC was composed semi-automatically.

Comparison With Aortic-LA M-Mode Echocardiography

The correlation between the LA volume curve and relative changes of the aortic posterior wall (PAW) motion on aortic-left atrial M-mode echocardiography is known.^{20,21} LA volume can be calculated from the M-mode LA dimension (LAD) using the curvilinear regression equation ($y = 1.4x^3 + 23$; y = LA volume (ml), x = M-mode LAD (mm)).²² In 16 patients (female, 4; male, 12; mean age, 60.8 ± 15.2 years; coronary artery disease, 13; dilated cardiomyopathy, 2; aortic regurgitation, 1), the correlation of ARV, PEV and AEV between the FVC and LA volume calculated from M-mode LAD was examined by simple regression analysis. A p value less than 0.05 was considered statistically significant.

LA Function

Patients were divided into 3 groups on the basis of the ratio of peak early filling velocity to peak atrial systolic velocity (E/A) in LVIF, the deceleration time of early filling flow (DcT) in LVIF, and the ratio of peak systolic velocity to peak diastolic velocity (S/D) in PVF. When $E/A \geq 1.0$, $DcT \geq 140$ ms, and $S/D \geq 1.0$, patients were classified as normal (N), when $E/A < 1.0$, patients were classified as abnormal (AB), and when $E/A \geq 1.0$, $DcT < 140$ ms, $S/D < 1.0$, patients were classified as pseudonormal (PN).²³⁻²⁵ ARV/SV, PEV/ARV, AEV/ARV, PEV/SV, and AEV/SV were compared among the 3 groups.

Using one-way ANOVA followed by Scheffe's F test, patient characteristics and the echocardiographic indices of each group were compared. Values were expressed as mean $\pm$ SD. A p value less than 0.05 was considered significant.

Results

FVC

The FVC shows a similar pattern to the LA volume curve shown in previous studies^{3-6,18} and could be divided into 4 phases as described previously⁵: an active filling phase in which the LA volume increased with LA relaxation and LV contraction; a passive emptying phase in which the LA volume decreased with LV early diastolic filling; a diastasis in which the LA volume changed slightly; and an active emptying phase in which the LA volume decreased with LA contraction (Fig 2).

Validity of FVC

Fig 3 is representative curves of the FVC and the PAW

Fig 3. Representative left atrial functional volume change curve derived from Doppler flow spectra (A) and the posterior aortic wall motion (B). PVF, pulmonary venous flow; LVIF, left ventricular inflow; PAW, aortic posterior wall; HR, heart rate.

motion; the 2 curves showed similar patterns. Fig 4A shows the correlation between the ARV derived from the FVC and that from the M-mode LAD, Fig 4B shows the correlation between the PEV derived from the FVC and that from the M-mode LAD, and Fig 4C shows the correlation between the AEV derived from the FVC and that from the M-mode LAD. Significant positive correlations were observed in ARV, PEV and AEV.

Comparison of the Parameters of LA Function

Table 1 shows the patient characteristics and echocardiographic parameters of the 3 groups. The mean age of the AB group was higher than that of the N group, but other parameters were not significantly different between the N and the AB group. The heart rate and the LA dimension in the PN group were higher than those in the N and AB groups, and the %FS in the PN group was significantly less than that in the N and the AB groups.

Representative FVCs of the N, AB, and PN groups are shown in Fig 5. Fig 6 shows the indices of the FVC in the 3

Fig 5. Representative left atrial functional volume change curve in normal (N), abnormal (AB), and pseudonormal (PN) groups. HR, heart rate.

Fig 4. Correlation of the parameters derived from Doppler flow spectra and the M-mode left atrial dimension. FVC, left atrial functional volume change curve derived from Doppler flow spectrums; ARV, atrial reservoir volume; PEV, passive emptying volume; AEV, active emptying volume.

groups. ARV/SV, AEV/ARV and AEV/SV were significantly greater in the AB group compared with the N group, whereas those of the PN group were significantly less than those of the N group. PEV/ARV and PEV/SV were significantly greater in the PN group than in N group, whereas that

Fig 6. Indices of left atrial function. Values are expressed as mean $\pm$ SD. * $p < 0.05$ vs N group, $^{\dagger}p < 0.05$ vs AB group. N, normal; AB, abnormal relaxation; PN, pseudonormal; ARV, atrial reservoir volume; SV, stroke volume; PEV, passive emptying volume; AEV, active emptying volume.

Table 1 Patient Characteristics and Echocardiographic Data

	N group (n=32)	AB group (n=67)	PN group (n=11)
Age (years)	50.2 $\pm$ 9.0	67.3 $\pm$ 9.8*	58.6 $\pm$ 13.0
Gender (M:F)	16:16	46:21	6:5
Heart rate (beats/min)	63.4 $\pm$ 9.1	67.9 $\pm$ 11.3	90.7 $\pm$ 22.0* †
LVEDD (mm)	47.0 $\pm$ 6.5	48.7 $\pm$ 7.0	48.3 $\pm$ 8.3
%FS (%)	37.5 $\pm$ 9.7	33.1 $\pm$ 10.3	18.3 $\pm$ 5.8* †
LAD (mm)	33.0 $\pm$ 4.3	33.7 $\pm$ 4.0	41.1 $\pm$ 4.3* †

Values are expressed as mean $\pm$ SD or number of patients. * $p < 0.05$ vs N group, $^{\dagger}p < 0.05$ vs AB group. N, normal; AB, abnormal relaxation; PN, pseudonormal; LVEDD, left ventricular end-diastolic dimension; %FS, %fractional shortening; LAD, left atrial dimension.

in AB group was significantly less than that in N group.

Discussion

In order to estimate LA function, the reservoir, conduit and booster pump functions should be separately estimated. For this purpose, it is important to know LA volume change curve and this study demonstrates that the FVC can be composed from Doppler signals, such as PVF and LVIF, and that it was a valid means of indicating LA volume change. Using parameters from the FVC, we then compared the LA function in normal, abnormal and pseudonormal LV relaxation groups defined by LVIF and PVF patterns. Compared with the normal group, the abnormal relaxation group showed increased LA reservoir and booster pump function indicated by ARV/SV and AEV/SV. On the other hand, the pseudonormal group had deteriorated LA reservoir and booster pump functions.

These results indicate that the abnormal relaxation group had a compensated increase in LA reservoir and booster pump function, which may assist in alleviating pulmonary congestion. On the other hand, the pseudonormal group had impaired LA reservoir and booster pump function, which may explain their vulnerability to pulmonary congestion, especially during tachycardia.

Methodological Considerations

In this study, to calculate the FVC, the PVF obtained from 1 PV instead of 4 was used. Earlier PVF studies reported that the VTIs of PVF between the right upper and left upper PV were not significantly different in the systolic and diastolic waves.²⁶ It has also been reported that ARV/SV in the left upper PV and right upper PV is similar.¹⁶ Thus, it is feasible to assume that the flow pattern of 1 PV represents the flow pattern of 4 PVs and it was assumed in this study that PV cross-sectional area did not change during 1 cardiac cycle. Although changes in PV shape and cross-sectional area during 1 cardiac cycle has been reported,^{13,27} the calculated PV volumetric spectrum (product of PV cross-sectional area and PVF spectrum) could be superimposed over the original PVF spectrum.¹³ Thus, it is reasonable to assume that PV cross-sectional area is constant for calculating the FVC.

It was also assumed that the mitral valve annular area did not change during ventricular diastole, although it has been shown that mitral valve annular area changes in shape and size during 1 cardiac cycle; however, the change is gradual and up to 12% from early to late diastole.²⁸ Therefore, it is possible to assume that the mitral valve annular area is constant during ventricular diastole for the purposes of calculating the FVC.

Comparison With Other Methods of Measuring the LA Volume Curve

Compared with other invasive and non-invasive calculation of the LA volume curve, such as left atrigraphy during cardiac catheterization, digital subtraction angiography and gated radionuclide atrigraphy, the FVC derived from Doppler signals is conveniently obtained and non-invasive. The PAW motion and the M-mode LAD may not accurately reflect the LA volume change when there is deformation of the aortic root or LA.

Study Limitations

When significant mitral regurgitation exists, accurate

measurement of inflow and outflow is disturbed and the FVC can not be correctly calculated. Without the simultaneous recording of LVIF and PVF, an irregular cardiac rhythm hinders the collection of Doppler signals of the beat with same R-R interval. Thus, in atrial fibrillation, the beat with same R-R interval should be selected. When the simultaneous recording of LVIF and PVF is possible, this problem will be solved.

Conclusions

We developed a new algorithm to obtain the FVC and from the indices of FVC we can demonstrate that in patients with an abnormal relaxation pattern, the LA reservoir and booster pump functions are both augmented and may compensate for impaired LV diastolic function; however, in patients with a pseudonormal pattern, LA reservoir and booster pump functions are both impaired. This dysfunction of LA may be related to an increase in ANP and subsequent vulnerability to pulmonary congestion.

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