DETERMINANTS OF LEFT ATRIAL SYSTOLIC TIME INTERVALS

— Assessment by Pulsed Doppler Echocardiography —

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To evaluate the responsible factors for left atrial ejection, the left atrial pre-ejection period (LAPEP), i.e., the time interval between atrial pacing pulse and onset of atrial ejection, and left atrial ejection time (LAET), i.e., the duration of atrial ejection, were determined from mitral inflow velocity patterns in 35 patients with various heart diseases using pulsed Doppler echocardiography. LAPEP ranged from 75 to 157 (mean 110 ± 18) msec and LAET from 80 to 169 (mean 124 ± 19) msec. The left atrial dimension before atrial contraction showed no significant correlation with LAPEP or LAET. Peak velocity during atrial contraction was negatively correlated with LAPEP ($r = -0.42$, $p < 0.05$) and positively with LAET ($r = 0.56$, $p < 0.01$). Left ventricular end-diastolic pressure (LVEDP) indicated a significant negative linear correlation with LAET ($r = -0.44$, $p < 0.05$). LAPEP showed no significant linear correlation with LVEDP, but a significant curvilinear relationship was observed between them ($\text{LAPEP} = 169 - 9 \cdot \text{LVEDP} + 0.28 \cdot \text{LVEDP}^2$, $r = 0.63$, $p < 0.001$). Mean pulmonary capillary wedge pressure (mPCWP) was curvilinearly related to LAPEP ($\text{LAPEP} = 168 - 11 \cdot \text{mPCWP} + 0.42 \cdot \text{mPCWP}^2$, $r = 0.72$, $p < 0.001$) and LAET ($\text{LAET} = 111 + 4.1 \cdot \text{mPCWP} - 0.22 \cdot \text{mPCWP}^2$, $r = 0.63$, $p < 0.001$). Although LAPEP decreased and LAET increased with increase in mPCWP up to about 15 mmHg, the reverse situation was noted for greater mPCWP. Thus, the major determinants of left atrial systolic time intervals are left atrial and ventricular pressures, and peak velocity during atrial contraction.

IT has been confirmed by many studies in experimental animals and humans that left atrial systole augments left ventricular filling and improves left ventricular performance to a significant degree.¹⁻⁵ Using ventriculography, it has been possible to assess atrial contribution to left ventricular filling

through volumetric study.⁵⁻⁸ M-mode and two-dimensional echocardiography and radionuclide angiography have also noninvasively provided information on the extent of atrial contribution to left ventricular filling.^{9,10} Recently, pulsed Doppler echocardiography has not only provided information about this contribution^{11,12} but has also indicated left atrial systolic time intervals (LASTI), i.e., left atrial pre-ejection period (LAPEP) and left atrial ejection time (LAET) in patients with hypertension.¹³

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Fig.1. Mitral flow patterns obtained by pulsed Doppler echocardiography and determination of the parameters. R=peak velocity in the rapid filling phase, A=peak velocity in the atrial contraction phase. PEP=left atrial pre-ejection period, ET=left atrial ejection time, P=right atrial pacing stimulus. TOWARD and AWAY=flow components toward and away from the transducer.

Fig.2. Relationship between left atrial ejection time and A/R ratio. A/R ratio=the ratio of peak velocity during atrial contraction to that during rapid filling.

Fig.3. LAPEP plotted against LVEDP. A curvilinear relationship is observed ($y=169-9x+0.28x^2$, $r=0.63$, $p<0.001$, $n=35$).

LASTI may possibly be influenced by afterload such as left ventricular end-diastolic pressure (LVEDP) and preload such as left atrial pressure, which is nearly equal to mean pulmonary capillary wedge pressure (mPCWP). The inter-relationships of these parameters have never been determined and LAPEP in the previous study was measured from the onset of a P wave in the electrocardiogram. However, determination of LAPEP from the start of the P wave is not always accurate. If atrial pacing is performed at a slightly higher rate than the sinus rate, the pacing pulse can be defined as the onset of electrical excitation of the atrium and LAPEP can be easily measured. The purpose of the present study is to clarify the determinants of LASTI using pulsed Doppler echocardiography during right atrial pacing at a slightly higher heart rate than the sinus rate with special attention to mPCWP and LVEDP.

METHODS

Study patients:

Thirty five patients with various heart diseases, 27 men and 8 women with a mean age of 55 ± 12 years, were used. A written informed consent was obtained from each patient and his or her family. There were 5 patients with dilated cardiomyopathy, 3 patients with hypertrophic cardiomyopathy, 9 patients with myocardial infarction, 12

Fig.4. LAET plotted against LVEDP. Arrows show patients with high LVEDP and small A/R ratio, indicating afterload mismatch in atrial ejection.

Fig.5. LAPEP plotted against mPCWP. The relationship between them was curvilinear ($y = 168 - 11x + 0.42x^2$, $r = 0.72$, $p < 0.001$, $n = 35$).

Fig.6. LAET plotted against mPCWP. The quadratic equation is, $y = 111 + 4.1x - 0.22x^2$, $r = 0.63$, $p < 0.001$, $n = 35$.

patients with angina pectoris and 6 patients with other heart diseases. All the patients showed sinus rhythm with normal PR intervals on the electrocardiogram and underwent cardiac catheterization. A 6F bipolar electrode catheter for right atrial pacing was inserted from the femoral vein and placed in the high lateral position of the right atrium near the sinus node. Right atrial pacing was performed at a rate of 60–100/min with an average of 73 ± 10 /min, which is a slightly higher than the sinus rate. A Swan-Ganz catheter was also inserted into another portion of the femoral vein and placed in the pulmonary artery. Mean pulmonary capillary wedge pressure was measured by the fluid filled system (Gould P23XL transducer). A pig tail catheter or a catheter tip manometer was inserted

from the femoral artery and placed in the left ventricle for measurement of LVEDP. MPCWP of the patients ranged from 5 to 25 mmHg with an average of 10 mmHg and LVEDP from 5 to 28 mmHg, the average being 14 mmHg. Ejection fraction estimated by left ventriculography ranged from 10 to 81% with an average of 56%.

Doppler recording. The ultrasound system used in the present study was a Toshiba SSH-40A/SDS-21A two-dimensional phased array sector scanner (Toshiba Medical Company, Tokyo, Japan) with a 2.4 MHz transducer. The pulse repetition rate was 4 kHz or 6 kHz. Doppler recording was performed during catheterization. The ultrasound transducer was placed at the cardiac apex to obtain an apical three-chamber-view. The sample volume was set in the mitral valve orifice and the left ventricular inflow velocity pattern was recorded at a paper speed of 50 or 100 mm/sec with a strip chart recorder (Toshiba LSR-20A). The peak velocity in the rapid filling phase (R), that in the atrial contraction phase (A), LAPEP (time interval from the pacing pulse to the onset of the left ventricular inflow in the atrial contraction phase) and LAET (duration of the atrial ejection flow) were determined from the left ventricular inflow velocity patterns in five consecutive cardiac beats (Fig. 1). The ratio A/R was also calculated. The ratio A/R is an index of atrial contribution to left ventricular filling during late diastole.

Left atrial dimension. Left atrial M-mode

echocardiogram at the aortic valve level was recorded by the conventional parasternal approach and left atrial dimension just before atrial contraction was measured.

Statistical analysis. Values were expressed as mean $\pm$ standard deviation. Linear and quadratic regression equations were derived using the method of least squares and correlation coefficient (r) for pairs of data. A probability (P) value of less than 0.05 was considered significant.

RESULTS

(1) LAPEP ranged from 75 to 157 (mean 110 ± 18) msec and LAET from 80 to 169 (mean 124 ± 19) msec. (2) The pacing rate and left atrial dimension before atrial contraction showed no significant correlation with LAPEP or LAET, while age showed a rough negative correlation with LAPEP ($r = -0.34$, $p < 0.05$) and a positive correlation with LAET ($r = 0.48$, $p < 0.01$). (3) The peak velocity during atrial contraction and A/R ratio were negatively correlated with LAPEP ($r = -0.42$, $p < 0.05$, $r = -0.35$, $p < 0.05$, respectively) and positively with LAET ($r = 0.56$, $p < 0.01$, $r = 0.61$, $p < 0.01$, respectively) (Fig. 2). (4) LVEDP had no significant linear correlation with LAPEP, but a significant curvilinear relationship was observed between them ($\text{LAPEP} = 169 - 9 \cdot \text{LVEDP} + 0.28 \cdot \text{LVEDP}^2$, $r = 0.63$, $p < 0.001$) (Fig. 3). LVEDP had a significant negative linear correlation with LAET ($r = -0.44$, $p < 0.05$) (Fig. 4). Three (all dilated cardiomyopathy) of 5 patients with LVEDP of more than 20 mmHg showed short LAET and had small A/R ratio and peak velocity during atrial contraction, indicating after-load mismatch in atrial ejection (arrows in Fig. 4). The remaining 2 patients with LVEDP of more than 20 mmHg showed normal LAET and they had large A/R ratio. (5) MPCWP showed a curvilinear relationship with LAPEP and LAET ($\text{LAPEP} = 168 - 11 \cdot \text{mPCWP} + 0.42 \cdot \text{mPCWP}^2$, $r = 0.72$, $p < 0.001$, $\text{LAET} = 111 + 4.1 \cdot \text{mPCWP} - 0.22 \cdot \text{mPCWP}^2$, $r = 0.63$, $p < 0.001$) (Fig. 5, 6). Although LAPEP decreased and LAET increased with increase in mPCWP up to a mPCWP of about 15 mmHg, this situation was reversed for greater mPCWP.

DISCUSSION

(1) Previous study on LASTI.

Recently, mitral inflow velocity patterns obtained by pulsed Doppler echocardiography have provided information not only on atrial contribution to left ventricular filling^{11,12} but also on left atrial ejection dynamics. Abe and his coworkers found that LASTI was able to be evaluated by pulsed Doppler echocardiography in patients with hypertension¹³. They noted patients with a fourth heart sound to have longer LAET and a shorter LAPEP than those without a fourth heart sound, and left ventricular wall thickness to be positively correlated with LAET. In the present study, the A/R ratio and peak velocity during atrial contraction in the mitral inflow velocity pattern were positively correlated with LAET and negatively correlated with LAPEP. Since an increase in the A/R ratio indicates a great left atrial contribution to left ventricular filling during late diastole, it may be related to occurrence of the fourth heart sound. Accordingly, the results obtained in the present study may support the previous findings. LAET was also correlated to age. Since the A/R ratio increases with aging,¹² LAET may also do so in elderly patients. According to Abe et al,¹³ the mechanism for longer LAET and shorter LAPEP in patients with a fourth heart sound is possibly an increase in the preload and afterload for atrial ejection. However, in their study, the parameters of afterload or preload were not determined. In the present study, we examined the direct relationship between LASTI and the left atrial afterload or preload, for example, LVEDP, mPCWP and left atrial dimension before atrial contraction. Moreover, Doppler recording was made at the same time as pressure measurement during catheterization.

(2) Determinants of LAET.

LAET was found to show a negative significant correlation with LVEDP and LAET to be very short in patients with marked elevation of LVEDP, as in cases with dilated cardiomyopathy. It has been reported that left and right ventricular ejections are influenced by the afterload^{14,15}. For example, patients with pulmonary hypertension, a high afterload against right ventricular ejection, have

short right ventricular ejection time!⁴ That is, the relationship between LAET and LVEDP appears essentially the same as that between right ventricular ejection time and pulmonary artery pressure. The patients with dilated cardiomyopathy and a marked elevation of LVEDP had short LAET, small A/R ratio and reduced peak velocity during atrial contraction. Thus, an afterload mismatch possibly exists in atrial ejection as in the case of ventricular ejection. However, 2 of the 5 patients with LVEDP of 20 mmHg or more had relatively long LAET in spite of high LVEDP. Since these 2 patients had large A/R ratio, a left atrial afterload mismatch may not be evident in them and it would seem that LAET does not always depend on the afterload but also possibly on the left atrial ejection volume.

(3) Determinants of LAPEP.

Taking into consideration atrioventricular pressure-cross-over during atrial contraction, LAPEP should become short in positive proportion to left atrial pressure, dp/dt of left atrial pressure during atrial contraction and ejection volume, and in negative proportion to left ventricular diastolic pressure. In the present study, LAPEP showed a curvilinear relation with LVEDP. The results of LAPEP in patients with high LVEDP (more than 20 mmHg) seem consistent with the foregoing hypothesis concerning atrioventricular pressure cross-over, i.e. when LVEDP is high, pressure cross-over during atrial contraction becomes later. No close relationship was observed between LAPEP and LVEDP in the normal range. These results indicate that many other factors influence LAPEP.

LAPEP also showed a curvilinear relationship with mPCWP as a factor of preload for left atrial ejection. That is, although LAPEP decreased with increase in mPCWP up to about 15 mmHg, it increased with greater mPCWP. The following may be a possible explanation for the curvilinear relationship between them; both LVEDP and mPCWP may influence LAPEP, but they mutually function in the opposite directions as mentioned above. Accordingly, the relation of LAPEP to LVEDP or mPCWP is very complicated. It is speculated that one of the determinants of LAPEP is left atrial pressure (nearly equal to mPCWP) when it is about

15 mmHg or less in the clinical setting. However, when mPCWP increases beyond 15 mmHg, LAPEP may be influenced by LVEDP rather than mPCWP, and it may increase again, as indicated by the relationship between LAPEP and LVEDP in patients with high LVEDP.

As shown here, LAPEP was negatively correlated with peak velocity during atrial contraction or the A/R ratio. Since the peak velocity and the A/R ratio obtained by pulsed Doppler echocardiography correlate well with ventricular volume changes during atrial contraction by radionuclide angiography,^{16,17} increased peak velocity and A/R ratio mean increased left atrial ejection volume. Accordingly, our results indicate that LAPEP may be influenced by atrial ejection volume, as is LAET.

Clinical implications and limitations. As shown in the present study, pulsed Doppler echocardiography is very useful for determining left atrial ejection dynamics. LASTI may be influenced by LVEDP, left atrial pressure and peak velocity during atrial ejection and afterload mismatch possibly exists in atrial contraction as noted for ventricular ejection. However, in the clinical setting, the influence of LVEDP and mPCWP on LASTI may be complicated, since they mutually function in the opposite directions.

Other factors possibly influencing LAPEP or LAET, such as positive inotropism or existence of intra-atrial conduction disturbance were not determined in the present study. They may possibly account for the weak correlation coefficients among parameters in the present study. The right atrial pacing may prolong the time interval between the pacing spike and atrial excitation, resulting in an increase in LAPEP, even in patients with normal PQ interval before pacing. This is one of the limitations of this study. However, the above-mentioned relations between LAPEP and LVEDP or mPCWP are considered to be certain, if the extent of pacing induced prolongation of LAPEP is constant.

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