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主論文

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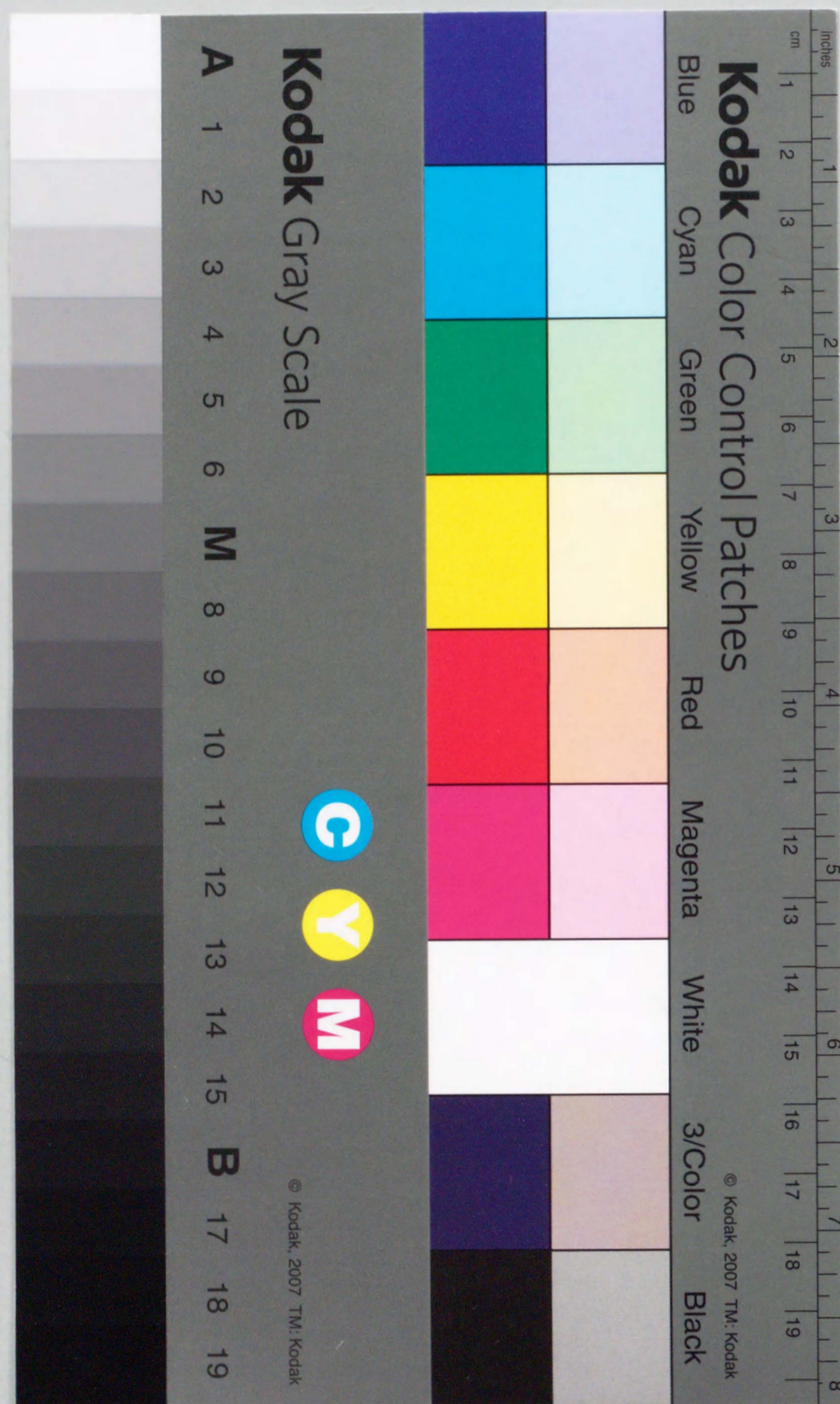
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**EFFECTS OF VASODILATORS ON PULMONARY VENOUS AND
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WITH CONGESTIVE HEART FAILURE**

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To characterize abnormalities in pulmonary venous flow velocity patterns and to explore the changes in these patterns following short-term (3 to 14 days) administration of vasodilators, pulmonary venous and mitral flow velocity patterns were serially studied at congestive heart failure and after vasodilator administration in 18 patients. Peak mitral early diastolic filling velocity (E) and the ratio of E to peak filling velocity at atrial contraction (E/A) consistently decreased after vasodilator administration by 30 ± 4 cm/s and 0.74 ± 0.13 (mean \pm SD), respectively. Peak pulmonary venous diastolic forward flow velocity also decreased by 29 ± 4 cm/s. However, changes in peak pulmonary venous systolic forward flow velocity (S, cm/s) did not correlate with changes in E, the E/A ratio, or D (peak pulmonary venous diastolic forward flow velocity). Thus, when patients were divided into two groups on the basis of changes in S, indices of left ventricular systolic performance, such as end-systolic dimension and fractional shortening, improved more in the group which showed an increase in S after vasodilator administration than in the group which showed a decrease in S (-7 ± 6 vs -1 ± 4 mm, $p < 0.05$; 8 ± 6 vs $-1 \pm 4\%$, $p < 0.05$). Although the mitral flow velocity pattern changed uniformly with vasodilator administration in patients with mild to moderate congestive heart failure, the changes in pulmonary venous flow velocity patterns were not uniform among patients. Pulmonary venous flow velocity patterns appear to reflect changes in left ventricular systolic performance in addition to those in left ventricular diastolic performance. (*Jpn Circ J* 1993; 57: 935–946)

VASODILATION therapy is one of the most important and popular treatments for congestive heart failure.^{1–3} Administration of vasodilators produces non-homogeneous alterations in hemodynamics and left ven-

tricular (LV) function, and pulsed Doppler measurements of mitral flow velocity patterns appear to be useful in assessing the beneficial effects of vasodilators on LV function.⁴ Recently, we and other groups suggested that an analysis of pulmonary venous flow velocity patterns may provide additional and complementary information for interpreting mitral flow velocity patterns.^{5–8} Therefore, the objectives of the present

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study were to characterize the abnormalities in pulmonary venous flow velocity patterns in patients with congestive heart failure and to explore the changes in pulmonary venous flow velocity patterns associated with vasodilator administration. Many physiological and pathological factors affect mitral flow velocity and, probably, pulmonary venous flow velocity patterns.^{9,10} Thus, in contrast to previous studies,^{11,12} the present study was focused exclusively on serial changes of Doppler echocardiographic parameters in patients with congestive heart failure before and after vasodilator administration. Thus, each patient served as his or her own control.

METHODS

Study population

The study population consisted of 18 patients with congestive heart failure who met the following criteria: (1) Adequate Doppler echocardiographic recordings of pulmonary venous flow velocity and mitral flow velocity patterns (3 cases excluded for this reason), (2) symptomatic (New York Heart Association functional class III or IV) congestive heart failure with pulmonary congestion on chest x-rays, (3) sinus rhythm with a heart rate of 100 bpm or less, (4) no evidence of moderate to severe mitral regurgitation as assessed by color Doppler flow imaging, (5) no valvular or congenital heart diseases, and (6) no asynergic LV wall motion. The subjects consisted of 12 men and 6 women who ranged in age from 40 to 77 years (mean 63). Etiology of congestive heart failure was hypertrophic heart disease in 9 patients, hypertensive heart disease in 5 patients, coronary artery disease in 3 patients, and dilated cardiomyopathy in 1 patient. Two patients had mild mitral regurgitation as assessed by color Doppler flow imaging at congestive heart failure. The same degree of mitral regurgitation was observed in the second ultrasound study.

All subjects gave their informed consent to the Doppler echocardiographic studies. The first Doppler echocardiographic study was performed at congestive heart failure, and the second study was performed 5 to 20 days later. Between the two Doppler echocardiographic studies, 10 patients received 40

to 80 mg of isosorbide dinitrate orally per day and 8 patients received 40 to 60 mg of nifedipine orally per day. At the second Doppler echocardiographic study, pulmonary congestion was not observed on any chest x-ray. Prior to each Doppler echocardiographic study, all subjects were examined using conventional two-dimensional and M-mode echocardiography to assess the chamber size, wall thickness and wall motion. The echocardiographic parameters were measured using standard methods from parasternal views.¹³

Doppler echocardiographic recordings

Pulsed Doppler echocardiographic recordings were obtained with a duplex Doppler echocardiograph (Toshiba SSH-160A) and a 2.5 MHz transducer array. A wall filter was set as low as possible, but it was not always possible to optimize velocity peaks in the recordings. Recordings were made with the subject in the left lateral position during quiet respiration. Velocity recordings were made at a paper speed of 100 mm/sec with simultaneous recording of the electrocardiogram and phonocardiogram. The phonocardiogram was recorded using a low pass filter with a contact microphone applied to the precordium where the aortic component of the second heart sound was loudest. This component was confirmed as the vibration which coincided with the aortic closing click recorded by Doppler echocardiography.

Pulmonary venous flow was examined from the apical four-chamber view. In the color Doppler mode, left atrial filling from the pulmonary vein can be recognized as red signals along the interatrial septum in the upper part of the left atrium. The pulsed Doppler sample volume was set just at the orifice of the right pulmonary vein, which appears at the bottom of these flame-like red signals. Following the pulmonary venous flow examination, mitral flow velocity patterns were obtained from the apical four-chamber view with the sample volume carefully placed between the tips of the mitral leaflets where the maximal flow velocity in early diastole was obtained.

Analysis of data

Flow velocity recordings were analyzed using a digitizing pad (GRAPHTEC, Tokyo,

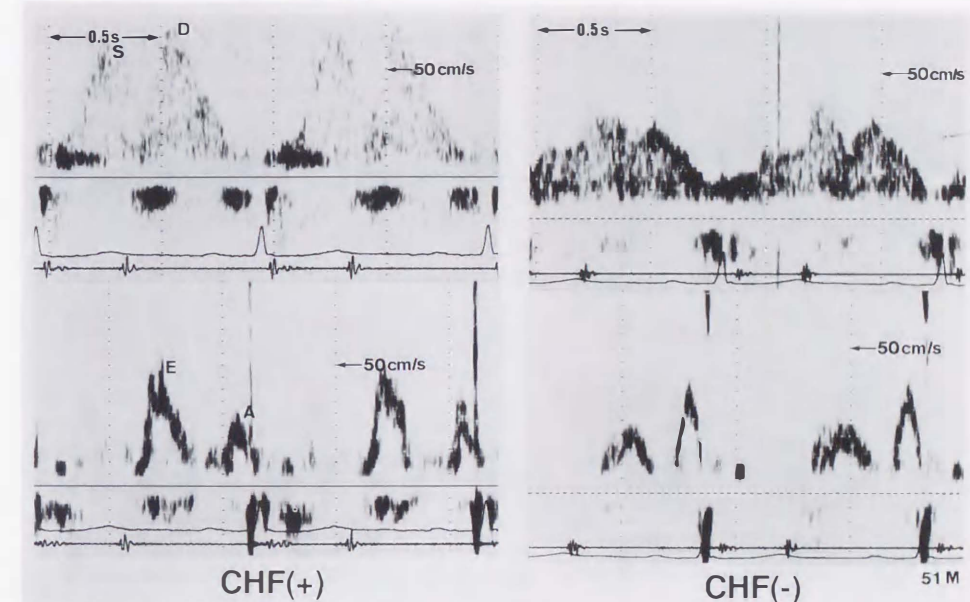


Fig. 1. Pulmonary venous flow velocity patterns (top panels) and mitral flow velocity patterns (bottom panels) at congestive heart failure (CHF)(left panels) and after vasodilator administration (right panels) in a 51-year-old male patient with dilated cardiomyopathy. Administration of vasodilator produced symptomatic improvement and disappearance of pulmonary congestion in the chest x-ray films. The mitral flow velocity pattern at congestive heart failure showed pseudonormalization with short isovolumic relaxation time, high peak early diastolic filling velocity (E) and low filling velocity at atrial contraction (A). In association with vasodilator administration, the pattern showed marked changes, including a decrease in E and increase in A. The pulmonary venous flow velocity pattern at congestive heart failure showed high peak systolic forward flow velocity (S) and high peak diastolic forward flow velocity (D). Both S and D decreased following vasodilator administration in this patient. Left ventricular systolic performance at congestive heart failure was considered normal even at congestive heart failure because fractional shortening of the left ventricular inner diameter was 26% at congestive heart failure.

Japan) interfaced with a computer system (NEC PC-9800, Tokyo, Japan) to measure time intervals, velocities and velocity integrals. The pulmonary venous flow velocity profiles were traced along the instantaneous highest velocity spectra by hand to determine peak forward flow velocities during systole (S) and diastole (D), peak reverse flow velocity at atrial contraction (A-pv), and flow velocity integrals of the systolic forward flow wave, the diastolic forward flow wave and the diastolic reverse flow wave. S and D were defined as the highest velocities during systole and diastole, respectively. A-pv was defined as the highest velocity during the atrial contraction phase. An increase in diastolic forward flow velocity began before systolic forward flow velocity had decreased to the zero baseline. Therefore, the flow

velocity integral of the systolic forward flow wave was defined as the area under the traced velocity profile from the onset of the forward flow to the onset of the diastolic forward flow wave (nadir), and the flow velocity integral of the diastolic forward flow wave was defined as the area from the onset of the diastolic forward flow wave to the end of the forward flow.

The mitral flow velocity profiles were traced along the instantaneous highest velocity spectra by hand to determine peak early diastolic filling velocity (E), peak filling velocity at atrial contraction (A), and the flow velocity integrals of the early diastolic filling wave and the filling wave at atrial contraction. E was defined as the highest velocity during the early diastolic filling period. A was defined as the highest velocity during

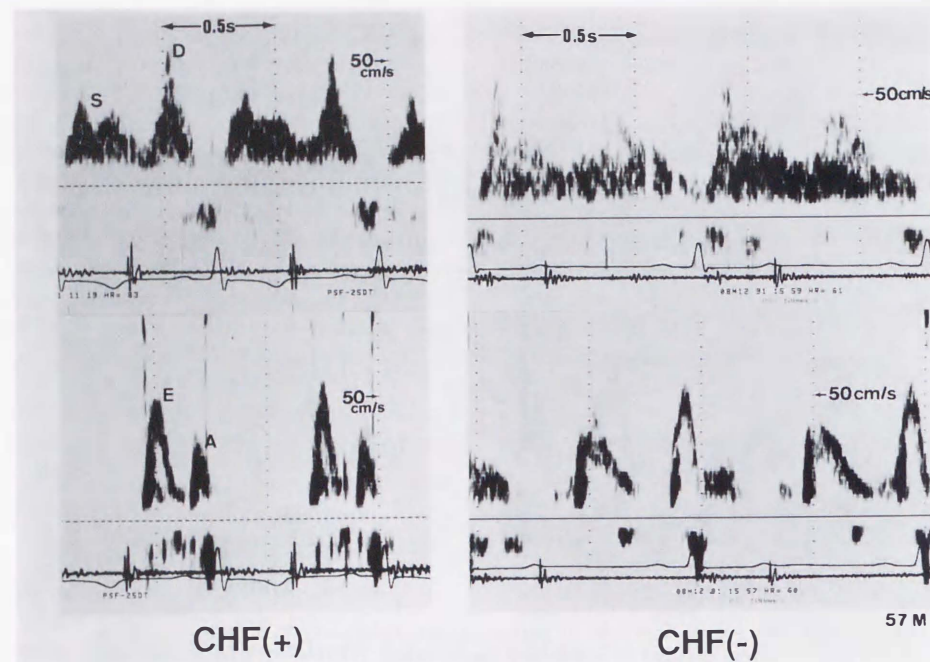


Fig. 2. Pulmonary venous flow velocity patterns (top panels) and mitral flow velocity patterns (bottom panels) at congestive heart failure (CHF)(left panels) and after vasodilator administration (right panels) in a 57-year-old male patient with hypertrophic heart disease. Administration of vasodilator produced symptomatic improvement, disappearance of pulmonary congestion in the chest x-ray films and an increase in the fractional shortening from 7 to 22%. The mitral flow velocity pattern at congestive heart failure showed pseudonormalization with short isovolumic relaxation time, high peak early diastolic filling velocity (E) and low filling velocity at atrial contraction (A). In association with vasodilator administration, the pattern showed marked changes, including a decrease in E and an increase in A. The changes in the mitral flow velocity pattern are similar to those observed in Fig. 1. The pulmonary venous flow velocity patterns at congestive heart failure showed low peak systolic forward flow velocity (S) and high peak diastolic forward flow velocity (D). D decreased following vasodilator administration in this case. In contrast to the patient in Fig. 1, S increased after vasodilator administration. Two peaks are noticeable during systole in pulmonary venous flow velocity patterns at both congestive heart failure and after vasodilator administration. Both of the systolic peaks decreased after vasodilator administration. This is the only case in which the first component of the systolic wave was higher than the second component.

the atrial contraction period. The flow velocity integral of the early diastolic filling wave was the area under the traced mitral flow velocity profile during the early diastolic filling period, and the flow velocity integral of the filling wave at atrial contraction was the area during the atrial contraction period. The average values of 5 to 7 consecutive cardiac cycles were used for quantitative analysis.

Statistical analysis

Results are expressed as mean values \pm SD. Differences in the variables between

subsets were assessed using analysis of variance and Scheffe's test. Statistical significance of the changes in the variables was assessed using analysis of variance and Scheffe's test for repeated measures. Chi-square analysis was used to assess the non-parametric data between subsets. Simple least-squares linear regression analysis was used to assess the correlation between two variables.

RESULTS

Changes in Doppler echocardiographic pa-

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TABLE 1 OVERALL CHANGES IN ECHOCARDIOGRAPHIC PARAMETERS ASSOCIATED WITH VASODILATOR ADMINISTRATION.

Status	before	after
HR (bpm)	71 \pm 17	67 \pm 13
SBP (mmHg)	173 \pm 33	138 \pm 18*
DBP (mmHg)	98 \pm 19	81 \pm 12*
Pulmonary venous flow velocity pattern		
S (cm/s)	53 \pm 23	48 \pm 14
D (cm/s)	64 \pm 17	38 \pm 9*
S/D	0.88 \pm 0.39	1.30 \pm 0.33*
A-pv (cm/s)	25 \pm 9	19 \pm 5*
FVI-S (cm)	12.0 \pm 4.9	11.8 \pm 4.6
FVI-D (cm)	11.9 \pm 3.9	10.0 \pm 3.6
FVI-S/D	1.02 \pm 0.34	1.41 \pm 0.82
FVI-A-pv (cm)	2.1 \pm 1.3	1.3 \pm 0.4*
Mitral flow velocity pattern		
IVRT (msec)	59 \pm 16	98 \pm 26*
E (cm/s)	77 \pm 17	48 \pm 14*
A (cm/s)	52 \pm 17	63 \pm 21
E/A	1.58 \pm 0.50	0.85 \pm 0.41*
Deceleration time (msec)	170 \pm 85	181 \pm 55
FVI-E (cm)	9.2 \pm 2.4	7.1 \pm 2.1*
FVI-A (cm)	4.3 \pm 1.9	5.3 \pm 1.6
FVI-E/A	2.44 \pm 0.88	1.44 \pm 0.55*
FVI-M (cm)	13.5 \pm 3.6	12.4 \pm 2.3
M-mode echocardiographic parameters		
LVDd (mm)	54 \pm 10	52 \pm 8
LVDs (mm)	41 \pm 12	38 \pm 9
FS (%)	26 \pm 11	28 \pm 9
LAD (mm)	40 \pm 6	35 \pm 5*

Values are expressed as the mean \pm SD. * p < 0.01 versus data before treatment. Abbreviations: A=peak filling velocity at atrial contraction; A-pv=peak reverse pulmonary venous flow velocity at atrial contraction; D=peak forward pulmonary venous flow velocity during diastole; DBP=diastolic blood pressure; E=peak early diastolic filling velocity; E/A=the ratio of peak early diastolic filling velocity to peak filling velocity at atrial contraction; FS=fractional shortening of the left ventricular inner diameter; FVI-A=flow velocity integral of diastolic filling at atrial contraction; FVI-A-pv=flow velocity integral of reverse pulmonary venous flow wave at atrial contraction; FVI-D=flow velocity integral of forward pulmonary venous flow wave during diastole; FVI-E=flow velocity integral of early diastolic filling; FVI-E/A=the ratio in flow velocity integral of early diastolic filling to flow velocity integral of diastolic filling at atrial contraction; FVI-M=mitral flow velocity integral over diastole; FVI-S=flow velocity integral of forward pulmonary venous flow wave during systole; FVI-S/D=the ratio of flow velocity integral of forward pulmonary venous flow wave during systole to that during diastole; IVRT=isovolumic relaxation time; LAD=left atrial dimension; LVDd=left ventricular end-diastolic dimension; S=peak forward pulmonary venous flow velocity during systole; SBP=systolic blood pressure; S/D=the ratio of peak forward pulmonary venous flow velocity during systole to that during diastole.

rameters associated with vasodilator administration

Fig. 1 and 2 show representative tracings of pulmonary venous flow and mitral flow velocity patterns at congestive heart failure and after vasodilator administration. In pulmonary venous flow velocity patterns, higher than normal D was observed at congestive heart failure. However, S at congestive

heart failure varied greatly. After vasodilator administration, D consistently decreased, but S increased in 8 patients and decreased in 10 patients. A biphasic systolic wave in the pulmonary venous flow velocity pattern was observed in 3 patients at congestive heart failure and in 4 patients after vasodilator administration. The second component of the systolic wave was higher than the first

TABLE II CHANGES IN ECHOCARDIOGRAPHIC PARAMETERS IN PATIENTS IN WHOM S INCREASED AND DECREASED FOLLOWING VASODILATOR ADMINISTRATION

Group	Increase in S	Decrease in S
Number	8	10
HR (bpm)	-2 ± 8	-8 ± 13
SBP (mmHg)	-37 ± 35	-34 ± 36
DBP (mmHg)	-27 ± 22	-9 ± 13
Pulmonary venous flow velocity pattern		
S (cm/s)	16 ± 8	$-23 \pm 13^*$
D (cm/s)	-28 ± 17	-25 ± 16
S/D	0.79 ± 0.21	$0.11 \pm 0.38^*$
A-pv (cm/s)	-4 ± 4	-7 ± 8
FVI-S (cm)	4.4 ± 1.9	$-3.9 \pm 6.0^*$
FVI-D (cm)	0.08 ± 5.7	-3.7 ± 3.6
FVI-S/D	0.68 ± 1.01	0.16 ± 0.82
FVI-A-pv (cm)	-0.5 ± 0.5	-1.0 ± 1.4
Mitral flow velocity pattern		
IVRT (msec)	51 ± 28	31 ± 14
E (cm/s)	-36 ± 16	-24 ± 10
A (cm/s)	21 ± 26	3 ± 12
E/A	-1.05 ± 0.51	$-0.47 \pm 0.30^*$
Deceleration time (msec)	33 ± 47	-6 ± 71
FVI-E (cm)	-2.2 ± 2.2	-2.1 ± 1.6
FVI-A (cm)	2.2 ± 2.2	0.2 ± 1.7
FVI-E/A	-1.42 ± 0.94	-0.65 ± 0.99
FVI-M (cm)	0.04 ± 2.8	-1.9 ± 2.3
M-mode echocardiographic parameters		
LVDd (mm)	-4 ± 5	-2 ± 6
LVDs (mm)	-7 ± 6	$-1 \pm 4^*$
FS(%)	8 ± 6	$-1 \pm 4^*$
LAD (mm)	-7 ± 4	$-3 \pm 3^*$

Values are expressed as the mean \pm SD. * $p < 0.01$ versus patients in whom S increased after vasodilator administration. Abbreviations: A=peak filling velocity at atrial contraction; A-pv=peak reverse pulmonary venous flow velocity at atrial contraction; D=peak forward pulmonary venous flow velocity during diastole; DBP=diastolic blood pressure; E=peak early diastolic filling velocity; E/A=the ratio of peak early diastolic filling velocity to peak filling velocity at atrial contraction; FS=fractional shortening of the left ventricular inner diameter; FVI-A=flow velocity integral of diastolic filling at atrial contraction; FVI-A-pv=flow velocity integral of reverse pulmonary venous flow wave at atrial contraction; FVI-D=flow velocity integral of forward pulmonary venous flow wave during diastole; FVI-E=flow velocity integral of early diastolic filling; FVI-E/A=the ratio of flow velocity integral of early diastolic filling to flow velocity integral of diastolic filling at atrial contraction; FVI-M=mitral flow velocity integral over diastole; FVI-S=flow velocity integral of forward pulmonary venous flow wave during systole; FVI-S/D=the ratio of flow velocity integral of forward pulmonary venous flow wave during systole to that during diastole; IVRT=isovolumic relaxation time; LAD=left atrial dimension; LVDd=left ventricular end-diastolic dimension; S=peak forward pulmonary venous flow velocity during systole; SBP=systolic blood pressure; S/D=the ratio of peak forward pulmonary venous flow velocity during systole to that during diastole.

component in all but 1 patient (Fig. 2). Mitral flow velocity patterns at congestive heart failure showed pseudonormalization with short or normal isovolumic relaxation times, high or normal E and low A. After vasodilator administration, the patterns showed marked changes, including a decrease in E and a slight increase in A.

Doppler echocardiographic results before and after vasodilator administration are summarized in Table I. Mean heart rates in the two ultrasound studies did not differ significantly. Mean S did not change after vasodilator administration, whereas D significantly decreased and the S/D ratio significantly increased after vasodilator administra-

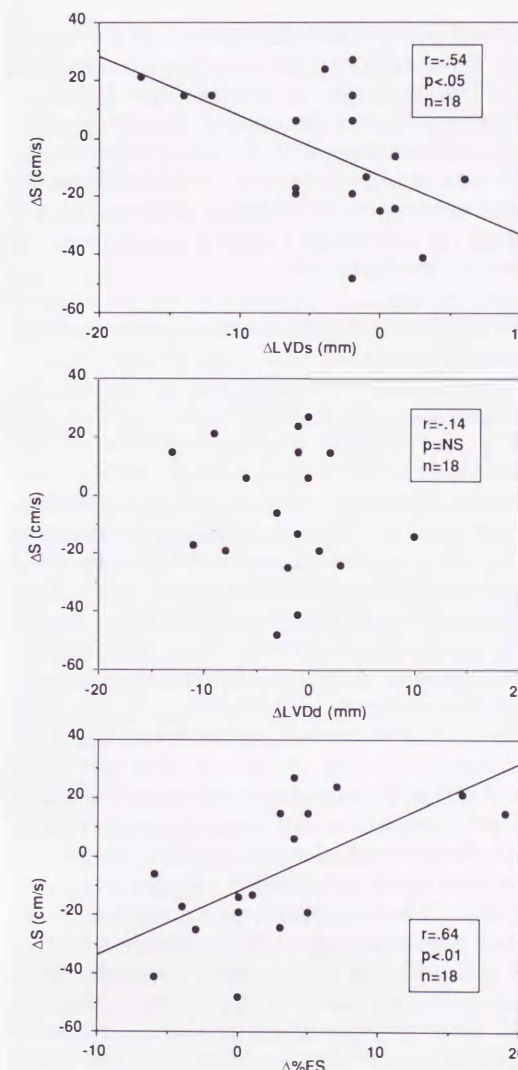


Fig. 3. Changes in peak pulmonary venous forward flow velocity during systole (S) were compared with changes in left ventricular end-systolic dimension (LVDs, in the top panel), left ventricular end-diastolic dimension (LVDd, in the middle panel), and fractional shortening (FS, in the bottom panel).

tion ($p < 0.01$, $p < 0.01$). A-pv and the flow velocity integral of the reverse pulmonary venous flow wave at atrial contraction decreased after vasodilator administration ($p < 0.01$, $p < 0.01$). Changes in mitral flow velocity patterns included lengthening of the isovolumic relaxation time ($p < 0.01$), de-

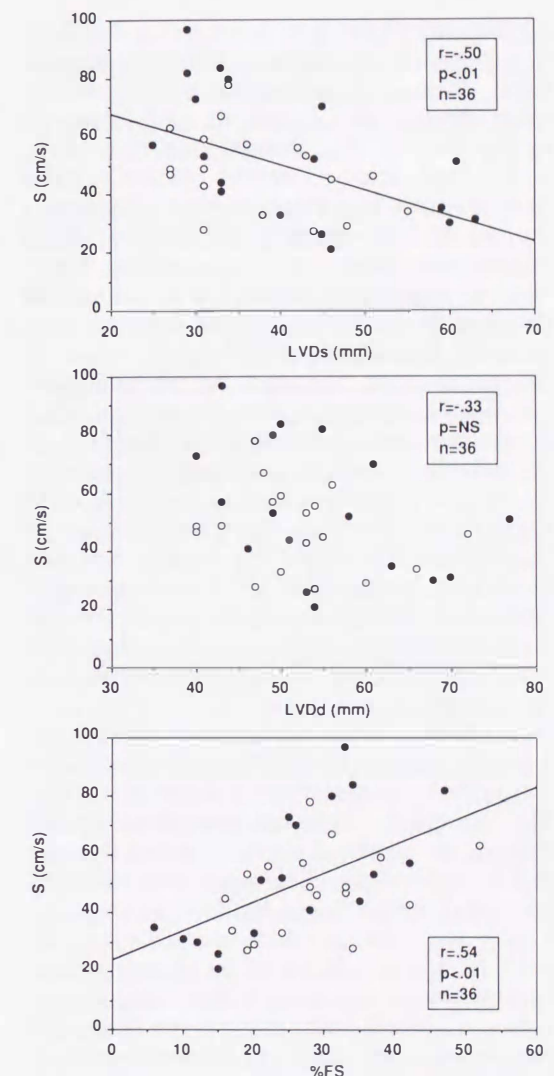


Fig. 4. Absolute values of peak pulmonary venous forward flow velocity during systole (S) were compared with left ventricular end-systolic dimension (LVDs, in the top panel), left ventricular end-diastolic dimension (LVDd, in the middle panel), and fractional shortening (FS, in the bottom panel). Closed and open circles denote data obtained at congestive heart failure and following vasodilator administration, respectively.

creases in E and the E/A ratio ($p < 0.01$, $p < 0.01$), and a constant A.

Subset study (Table II)

We divided the patients into two subsets on the basis of changes in S: 8 patients showed an increase in S (S_{inc}) and the other

10 patients showed a decrease in S (S_{dec}). S_{inc} consisted of 4 patients with hypertrophic heart disease, 2 patients with hypertensive heart disease and 2 patients with coronary artery disease. S_{dec} consisted of 5 patients with hypertrophic heart disease, three patients with hypertensive heart disease, a patient with coronary artery disease and a patient with dilated cardiomyopathy. There was no significant difference between the distribution of diseases in the subsets. Due to space limitations, the absolute values of the parameters measured before and after vasodilator administration are not reported here. However, complete list of these values is available in tabular form from the authors on request. Changes in S/D and E/A were significantly larger in S_{inc} patients than in S_{dec} patients. Similarly, changes in echocardiographic parameters of LV end-systolic dimension, fractional shortening of the LV inner diameter and left atrial dimension were significantly larger in S_{inc} patients than in S_{dec} patients.

In addition to the subset study, changes in S were compared with changes in echocardiographic parameters of LV function (Fig. 3). Changes in S correlated significantly with changes in fractional shortening and changes in LV end-systolic dimension, but not with LV end-diastolic dimension ($r=.64$, $p<0.01$, $n=18$; $r=-.54$, $p<0.05$, $n=18$; $r=-.14$, $p=N.S.$, $n=18$). None of the changes in the parameters of the mitral flow velocity pattern correlated with changes in fractional shortening or LV end-systolic/diastolic dimensions. Absolute values of S before and after vasodilator administration also correlated with absolute values of fractional shortening and LV end-systolic dimension ($r=.54$, $p<0.01$, $n=36$; $r=-.50$, $p<0.01$, $n=36$ in Fig. 4).

DISCUSSION

In this study, characteristics of abnormal pulmonary venous flow velocity patterns in congestive heart failure were established by serial Doppler echocardiographic studies before and after vasodilator administration. Our data indicate that D and A-pv uniformly increase at congestive heart failure, whereas S does not. Vasodilator administration produced uniform changes in parameters of pul-

monary venous diastolic flow wave and mitral flow velocity patterns in patients with mild to moderate congestive heart failure. However, the pulmonary venous systolic flow wave changed in various ways among the patients. The pulmonary venous systolic flow wave appears to reflect changes in LV systolic performance rather than those in LV diastolic performance.

Mitral flow velocity patterns in congestive heart failure

Vasodilator administration produced significant changes in mitral flow velocity patterns. Isovolumic relaxation time was prolonged, E and the E/A ratio decreased and deceleration time was prolonged. Shortening or normalization of isovolumic relaxation time, increases in E and the E/A ratio and shortening of deceleration time have been previously reported in patients with congestive heart failure.^{11,14,15} Thus, in terms of the effects of congestive heart failure on mitral flow velocity patterns, our results are consistent with previously described findings.

Vasodilator administration did not produce a significant change in mean fractional shortening of the LV inner diameter. LV end diastolic dimension slightly decreased and left atrial dimension significantly decreased after vasodilator administration. These findings suggest that reduction of the LV preload was the primary hemodynamic change in our patients. Changes in the mitral flow velocity pattern associated with vasodilator administration included decreases in E and the E/A ratio and a slight increase in A. These results imply that characteristic changes in mitral flow velocity patterns in congestive heart failure can be attributed to the load dependency of the mitral flow velocity pattern.¹⁴⁻¹⁸ In other words, the characteristic mitral flow velocity patterns in mild to moderate congestive heart failure may be largely due to abnormal loading conditions. In this context, our results are consistent with those obtained by Vanoverschelde and his colleagues,¹⁵ who found a close relation between the E/A ratio and mean pulmonary capillary wedge pressure in patients with congestive heart failure.

The effects of vasodilators on mitral flow velocity patterns have been previously studied in patients with extreme congestive heart

failure.⁴ The findings of the present study are in contrast to those of the previous study⁴ which showed inconsistent changes in E despite uniform decreases in pulmonary capillary wedge pressure. The discrepancy between these two studies may be due to the difference in the severity of congestive heart failure of the patients. In the previous study, constant E despite preload reduction was explained by the associated changes in extracardiac constraints. Because all of our patients had only mild to moderate congestive heart failure, the extracardiac constraints were unlikely to be increased even at congestive heart failure.

Pulmonary venous flow velocity patterns in congestive heart failure

Pulmonary venous flow velocity patterns in patients with congestive heart failure were obviously different from those in normal subjects. D was even higher than our previously reported normal value and the S/D ratio was even lower than our earlier normal value.⁶ These findings suggest that an analysis of pulmonary venous flow velocity patterns is useful for confirmation of clinically suspected congestive heart failure even in patients with pseudonormalized mitral flow velocity patterns. Vasodilator administration produced significant decreases in D and A-pv and a significant increase in the S/D ratio. Since the left atrium acts as a conduit in diastole, pulmonary venous diastolic flow should largely reflect mitral flow.⁹ In the present serial ultrasound studies, a decrease in D was associated with a decrease in E.

We previously suggested that A and A-pv are affected by atrial ejection function and by the balance between the impedance of the left ventricle and that of the pulmonary venous system.⁶ Although A tended to increase after vasodilator administration, A-pv significantly decreased after vasodilator administration. This apparent paradox regarding the changes in the flows caused by atrial contraction can be explained by the fact that impedance of the pulmonary venous system is less pressure-dependent than that of the left ventricle.²⁰ The impedance of the left ventricle may decrease more with vasodilator administration than does the impedance of the pulmonary venous system. With regard to the serial changes in A, the effect

of a decrease in atrial ejection function due to decreased preload (Frank-Starling principle of the atrium) may have been overcome by the associated decrease in the impedance of the left ventricle.

Pulmonary venous systolic forward flow wave

To clarify the factors which regulate changes in S, the patients were divided into two subsets on the basis of the changes in S, and parameters of the subsets were compared. The results of the subset study indicated that an increase in S following vasodilator administration was associated with improvements in the parameters of LV systolic performance, such as L.V end-systolic dimension and fractional shortening, while a decrease in S was associated with little or no changes in the parameters of LV systolic performance. There were no significant differences in any of the parameters that reflect changes in left atrial pressure, such as D, isovolumic relaxation time and E, suggesting that the decrease in left atrial pressure associated with vasodilator administration was comparable between the subsets. Because LV systolic performance and left atrial pressure are independent key variables in assessing the hemodynamic profile of congestive heart failure, measurements of the pulmonary venous systolic flow wave may provide information related to LV systolic performance rather than left atrial pressure. This suggestion contrasts with the finding that measurements of the pulmonary venous diastolic flow wave may provide information related exclusively to left atrial pressure.

The possible contribution of LV systolic performance to S is supported by the results of our correlation studies (Fig. 3 and 4) because both absolute values of S and their changes correlated well with the absolute values and the changes of the parameters of LV systolic performance. These findings may be comparable to the recent finding of Nishimura and his colleagues.⁵ They showed that changes in systolic forward flow velocity in the pulmonary vein were directly proportional to changes in cardiac output. On the other hand, our present finding apparently contradicts the results of Kuecherer et al.²¹ who found a strong correlation between the systolic fraction of pulmonary venous flow

and mean left atrial pressure. Their study was performed using subjects with normal LV systolic function, and this difference in the study populations may explain the discrepancy between Kuecherer's study and ours.

Transthoracic versus transesophageal approach

It is currently believed that pulmonary venous flow velocity patterns which are obtained using transthoracic and transesophageal approaches are primarily different in the following two points^{6,7,22}. First, biphasic systolic components are consistently observed in transesophageal Doppler echocardiographic recordings while a lone peak is observed in systole in about 70% of the subjects in transthoracic Doppler echocardiographic recordings⁶. Thus, it was not clear in this study whether the first or second component of the systolic wave contributed to the results of this study, although we believe that the second component is more likely. Second, it is difficult to obtain adequate recordings of the pulmonary venous reversal flow wave at atrial contraction with the transthoracic approach. Thus, we did not emphasize the change in the reversal flow wave although Nishimura and his colleagues suggested the value of analyzing this wave⁵.

A transthoracic approach, if possible, is no doubt better than a transesophageal approach because of its noninvasiveness. However, the percentage of technically inadequate studies using this technique can reach as high as about 20%⁶. Ultrasound equipment has been improving year by year, and it should be much easier to obtain acceptable pulmonary venous flow velocity recordings in most patients in the near future. Otherwise, intravenous use of a contrast medium that passes pulmonary beds should decrease the number of technically inadequate studies^{23,24}.

Limitation of the study

Several limitations of the study are noted. First, hemodynamic or pressure data were not available in this study. Although these data were not measured in this study, all patients had obvious pulmonary congestion on the chest x-ray film at congestive heart failure, which strongly suggests high left atrial

pressure. Disappearance of pulmonary congestion after vasodilator administration indicates a decrease in left atrial pressure. Furthermore, the hemodynamic effects of the vasodilators we used are well known. Thus, lack of hemodynamic or pressure data does not invalidate this study which was focused on serial changes in Doppler echocardiographic parameters.

Second, either isosorbide nitrate or nifedipine was used as a vasodilator drug in our patients. It is known that these drugs have different actions as vasodilator drugs because isosorbide nitrate dilates primarily veins while nifedipine dilates primarily arteries. Thus, the hemodynamic responses to these drugs may very well differ. An arteriodilator is more likely to improve LV systolic performance than a venodilator. Although the percentages of patients receiving isosorbide nitrate and nifedipine were similar in the S_{mc} and S_{dec} subsets, the differences between the response of LV systolic function and, hence, of the pulmonary venous flow velocity pattern among the patients may be at least partially explained by the differences in the drug administered.

Third, 14 of 18 patients had hypertrophic and hypertensive heart disease, and measurements at congestive heart failure state were consistent with only mild LV systolic dysfunction (LV end diastolic inner diameter=54 mm; mean fractional shortening=26%). On the other hand, fractional shortening was less than 20% in 6 patients. These data indicate that our patient population was non-homogeneous with regard to the primary phase of ventricular dysfunction, i.e., systole or diastole. The percentage of patients with congestive heart failure due primarily to diastolic dysfunction is higher in this study than is usually seen in clinical practice.

Fourth, two patients with mild mitral regurgitation were included in this study. Some researchers have shown that pulmonary venous flow velocity patterns are only minimally affected by mild mitral regurgitation, if present, although they are significantly affected by severe mitral regurgitation²⁵⁻²⁷. Because patients with moderate to severe mitral regurgitation were not included in our study, inclusion of two patients with mild mitral regurgitation is unlikely to have

affected the conclusion of this study. However, the pulmonary venous systolic flow wave may decrease or even be absent or reversed in the presence of severe mitral regurgitation. Thus, we should be aware of this limitation when applying our data to the interpretation of pulmonary venous flow velocity recordings.

Finally, most of our patients showed a significant decrease in heart rate associated with vasodilator administration. Although it is believed that changes in heart rate of 10 bpm or so are unlikely to significantly affect pulmonary venous flow velocity patterns, the effects of heart rate on pulmonary venous flow velocity patterns are still unknown.

Clinical implications

Based on the findings of the present study, we can propose a simple noninvasive method for assessing congestive heart failure. High systolic and diastolic pulmonary venous forward flow velocities in patients with congestive heart failure imply little or no deterioration in LV systolic performance. Low pulmonary venous systolic forward flow velocity with high diastolic forward flow velocity implies the presence of LV systolic dysfunction. Low pulmonary venous diastolic forward flow velocity implies the absence of congestive heart failure.

Although the values obtained by a single ultrasound examination might be useful for confirmation of clinically suspected congestive heart failure and for the assessment of congestive heart failure, comparative studies should facilitate more reliable and accurate assessment of congestive heart failure. Furthermore, measurements of pulmonary venous flow velocity patterns obtained with transthoracic Doppler echocardiography can be easily repeated to observe the effects of treatment. An increase in the pulmonary venous systolic forward wave with a decrease in the diastolic forward wave in serial studies suggests a decrease in LV preload and a concomitant improvement in LV systolic performance. If both the systolic and diastolic flow waves decrease in serial studies, a significant improvement in LV systolic performance may not be associated with LV preload reduction. Thus, analysis of serial pulmonary venous flow velocity patterns was considered to be particularly useful in assess-

ing the effects of vasodilators in patients with congestive heart failure.

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