

Angiotensin-Converting Enzyme (ACE) Inhibitors Revert Abnormal Right Ventricular Filling in Patients With Restrictive Left Ventricular Disease

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Objectives. Our aim was to determine mechanisms underlying abnormalities of right ventricular (RV) diastolic function seen in heart failure.

Background. It is not clear whether these right-sided abnormalities are due to primary RV disease or are secondary to restrictive physiology on the left side of the heart. The latter regresses with angiotensin-converting enzyme inhibition (ACE-I).

Methods. Transthoracic echo-Doppler measurements of left- and right-ventricular function in 17 patients with systolic left ventricular (LV) disease and restrictive filling before and 3 weeks after the institution of ACE-I were compared with those in 21 controls.

Results. Before ACE-I, LV filling was restrictive, with isovolumic relaxation time short and transmitral E wave acceleration and deceleration rates increased ($p < 0.001$). Right ventricular long axis amplitude and rates of change were all reduced ($p < 0.001$), the onset of transtricuspid Doppler was delayed by 160 ms after the pulmonary second sound versus 40 ms in normals ($p < 0.001$) and overall RV filling time reduced to 59% of total diastole. Right ventricular relaxation was very incoordinate and peak E

wave velocity was reduced. Peak RV to right atrial (RA) pressure drop, estimated from tricuspid regurgitation, was 45 ± 6 mm Hg, and peak pulmonary stroke distance was 40% lower than normal ($p < 0.001$). With ACE-I, LV isovolumic relaxation time lengthened, E wave acceleration and deceleration rates decreased and RV to RA pressure drop fell to 30 ± 5 mm Hg ($p < 0.001$) versus pre-ACE-I. Right ventricular long axis dynamics did not change, but tricuspid flow started 85 ms earlier to occupy 85% of total diastole; E wave amplitude increased but acceleration and deceleration rates were unaltered. Values of long axis systolic and diastolic measurements did not change. Peak pulmonary artery velocity increased ($p < 0.01$).

Conclusions. Abnormalities of RV filling in patients with heart failure normalize with ACE-I as restrictive filling regresses on the left. This was not due to altered right ventricular relaxation or to a fall in pulmonary artery pressure or tricuspid pressure gradient, but appears to reflect direct ventricular interaction during early diastole.

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Right atrial (RA) pressure is often raised in patients with severe left ventricular (LV) disease, giving rise to the clinical picture of congestive heart failure. In some cases, this may reflect the presence of significant functional tricuspid regurgitation, but more frequently it is due to high right ventricular (RV) diastolic pressures. It is likely to be particularly prominent when LV filling is restrictive (1). Previous studies in patients with dilated cardiomyopathy have demonstrated abnormalities in RV filling that may be depressed during early diastole and associated with striking incoordination when correlated with RV wall motion (2,3). It remains unclear whether these changes represent the effects of previous diastolic RV disease, abnormal loading due to elevated left atrial

and thus pulmonary artery pressure, or some other mechanism. It was the purpose of the present study to investigate this question by studying interrelations between diastolic events on the right and left sides of the heart in a group of patients with severe LV disease, and to observe how these relations were modified by treatment with angiotensin-converting enzyme inhibition (ACE-I).

Methods

We studied 17 consecutive patients (age 60 ± 10 years) who conformed to the following criteria: 1) A diagnosis of heart failure requiring treatment with ACE-I on purely clinical grounds. 2) Evidence of LV systolic disease, with an end diastolic dimension greater than 5.8 cm, the upper 95% confidence interval (CI) of normal, and a shortening fraction less than 20%. 3) A restrictive filling pattern as assessed by pulsed echo-Doppler with an E/A ratio >1 and an E wave deceleration time <120 ms. 4) Satisfactory echo-Doppler records from both sides of the heart. No patient had uncor-

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Abbreviations and Acronyms

ACE-I	=	angiotensin converting enzyme inhibition
LA	=	left atrial
LV	=	left ventricular
P2	=	pulmonary component of the second sound
RA	=	right atrial
RV	=	right ventricular

rected structural valve disease, pericardial disease or pulmonary disease, and all were in sinus rhythm. Mild functional mitral regurgitation was noted in 13 patients. No patient had significant wall motion abnormality. The underlying cardiac disease was coronary artery disease in eight patients, idiopathic dilated cardiomyopathy in three patients, aortic valve replacement in two patients, hypertension in two patients, sarcoidosis in one patient (with no evidence of cor pulmonale) and in the remaining patient it was unknown. The ACE-I prescribed and its dose were determined by the referring physician; captopril was given to eight patients, enalapril to four patients and lisinopril to five patients. All patients were studied by echocardiography before and 3 weeks after starting treatment. Between the two echocardiographic studies other drugs were not altered.

Twenty-one normal subjects, age 58 years (SD 11 years), served as controls. They were studied by the same operators and over the same time period as the study patients. None had a history of shortness of breath, hypertension, valvular or ischemic disease or pulmonary disease.

All patients were studied at rest. We obtained cross sectional two-dimensional (Andover, Massachusetts) guided M modes and Doppler velocities using a Hewlett Packard Sonos 1500 system with a 2.5 MHz transducer. With the patient lying in the left semilateral position, M modes of the LV minor axis were recorded from the parasternal long axis view with the cursor at the tips of mitral valve leaflets. Long axis M-mode recordings of RV free wall were obtained with the cursor positioned at the tricuspid valve annulus (2). All records were made during quiet expiration. Transmitral and transtricuspid Doppler flow velocities were obtained using the same echocardiograph within 5 min of one another with the sample volume at the tips of mitral and tricuspid valve leaflets in the apical four-chamber view. Aortic and pulmonary outflow tract velocities were recorded with the pulsed-Doppler sample volume at the valve tips from the parasternal short axis view and apical four-chamber view, respectively. Continuous wave Doppler traces of mitral and tricuspid regurgitation were recorded using a Doptek system (Colchester, UK), with a 2.5 MHz nonimaging transducer. The apexcardiogram was recorded using Cambridge equipment (time constant 4 s). An electrocardiogram and phonocardiogram were recorded superimposed on all M-mode, Doppler and pulse traces which were photographically recorded at a paper speed of 100 mm/s. M-mode traces were later digitized off line using a dedicated computer program (4).

Measurements. End diastolic LV dimensions were taken at the onset of the q wave of the electrocardiogram (ECG), and end systolic dimensions were taken at the first high-frequency component of the aortic component of the second heart sound (A2) of the phonocardiogram. Left ventricular fractional shortening was estimated as the percentage fall in dimension during ejection with respect to end diastolic dimension. Iso-volumic relaxation time was measured from the mitral valve echogram as the time interval between A2 and the onset of mitral cusp separation. Right ventricular, long axis total excursion was measured from the innermost point (at end systole) to the outermost point (at end diastole). The A wave was taken as the extent of additional long axis motion between the end of the P wave of the ECG and the onset of the succeeding systole. Incoordinate relaxation was measured as the amplitude of abnormal movement after A2 or P2 (the pulmonary second sound), during early diastole, before the onset of mitral or tricuspid flow motion, respectively, towards the ventricular apex being expressed as positive and toward the atria as negative. The identities of A2 and P2, the aortic and pulmonary components of the second heart sound, were routinely checked against the corresponding valve closure artifact on the aortic and pulmonary Doppler flow velocity traces. From the digitized traces, peak LV minor axis and RV, long axis shortening (in systole) and lengthening (in diastole) were measured as well as the time interval between the q wave and peak shortening rate and the second heart sound, A2 or P2, and peak lengthening rate.

From the transmitral and transtricuspid pulsed-Doppler traces, peak early and late diastolic filling velocities were measured and the E/A ratio calculated. Total LV and RV filling times were measured as the total duration of transmitral and transtricuspid flow, respectively, and the ratio of each to total diastolic time calculated. Total diastolic time itself was measured as the period between the onset of P2 and the onset of the q wave of the ECG of the succeeding beat. Mitral and tricuspid E-wave acceleration times were measured from onset to peak velocity, and mean acceleration rates as peak velocity divided by corresponding acceleration time. Deceleration times and rates were measured in the same way on both sides of the heart, the former being derived by extrapolation if the A wave was partially superimposed on the descending limb of the E wave. A wave velocity was measured with respect to baseline. Pressure gradients in $\text{mm Hg}\cdot\text{cm}^{-1}$ were calculated as $0.075 \times$ acceleration rate in $\text{m}\cdot\text{s}^{-2}$. Right ventricular to RA systolic pressure drop was measured from the peak tricuspid regurgitation velocity as assessed by continuous wave Doppler and presented in mm Hg, using the simplified Bernoulli equation. Peak LV and RV outflow tract velocities were measured from the pulsed-Doppler trace. Aortic and pulmonary total ejection times were measured from the same trace, and stroke distance was derived. The percentage of end diastolic A wave amplitude to total pressure amplitude was measured from the apexcardiogram.

Statistics. Values are expressed as mean \pm SD. Patients' values before treatment with ACE-I were compared with

Table 1. Left Ventricular Inflow and Outflow Tract Doppler Velocities and Timing

Variables	Controls (n = 21)	Patients (n = 17)	
		Pre-ACE-I	With ACE-I
R-R interval (ms)	940 ± 200	715 ± 145	790 ± 180
Isovolumic relaxation time (ms)	60 ± 10	11 ± 17**	82 ± 40†
Mitral Doppler			
A2-onset of mitral flow (ms)	80 ± 15	60 ± 17**	120 ± 30†§
Peak E wave velocity (cm/s)	70 ± 10	86 ± 17	47 ± 20†§
E acceleration time (ms)	75 ± 10	66 ± 13	79 ± 15
E acceleration rate (m·s ⁻²)	10 ± 2.0	13.5 ± 4.0**	6.7 ± 3.0†§
Early diastolic pressure gradient (mm Hg/cm)	0.75 ± 0.1	1.01 ± 0.1**	0.5 ± 0.1†§
E deceleration time (ms)	160 ± 20	73 ± 19**	120 ± 30†§
E deceleration rate (m·s ⁻²)	4.6 ± 1.6	12 ± 4**	4.7 ± 2†
Peak A wave velocity (cm/s)	50 ± 10	32 ± 26*	75 ± 20†§
E/A ratio	1.4 ± 0.4	2.7 ± 1.8*	0.8 ± 0.9†‡
Total filling time (ms)	380 ± 125	286 ± 85*	320 ± 100
Total diastolic time (ms)	430 ± 20	345 ± 100**	410 ± 150
Filling/diastolic time (%)	88 ± 10	83 ± 12	79 ± 11
Apexcardiogram			
A wave/total pressure (%)	15 ± 5	48 ± 20**	16 ± 7†
Peak aortic velocity (cm/s)	110 ± 20	100 ± 40	90 ± 35
Total ejection time (ms)	240 ± 20	238 ± 29	240 ± 25
Aortic stroke distance (cm·s ⁻²)	12.2 ± 2.0	12.3 ± 7.0	11.1 ± 4

*p < 0.01; **p < 0.001 patients before ACE-I vs. controls (unpaired *t* test); †p < 0.001 patients with ACE-I vs. before ACE-I (paired *t* test); ‡p < 0.01; §p < 0.001 patients after ACE-I vs. controls (unpaired *t* test). ACE-I = angiotensin-converting enzyme inhibition.

controls using unpaired Student *t* test. Patient data before and after treatment were compared using a paired *t* test. In view of multiple *t* tests, a Bonferroni correction was implemented and the statistical significance was taken to apply when p value was less than 0.017.

Results

Before ACE-I (Tables 1 to 3). *Left ventricle.* By definition, the LV cavity was dilated. Mean end diastolic dimension proved to be 7.1 ± 1.2 cm and fractional shortening was low, 14% ± 2.5%. Left ventricular isovolumic relaxation time was short, being reduced to 25% normal value (p < 0.001 vs. normal). Transmitral Doppler showed increased acceleration and deceleration rates, particularly the latter by a factor of nearly 3 (p < 0.001 vs. normal). Total LV filling time was approximately 100 ms shorter than that in normals (p < 0.01), as was total diastolic time, so their ratio remained within the normal range. Peak aortic velocity, total ejection time and aortic stroke distance were all normal. Pressure A wave on the apexcardiogram was raised to almost 50% of the total displacement (p < 0.001 vs. normal) (Table 1).

Right ventricle. Total systolic excursion of RV long axis was 40% lower than normal, and peak shortening rate was 25% lower (p < 0.001 for both vs. normal). The time interval between the q wave of the ECG and the timing of peak shortening rate was not different between patients and controls. The degree of RV, long axis lengthening between P2 and the onset of tricuspid flow was much greater in patients (p <

0.01 vs. normal), particularly when expressed as a percentage of total excursion. The peak rate of RV, long axis lengthening was low in patients (p < 0.001 vs. normal), and the peak value itself occurred early in respect to P2 (p < 0.001 vs. normal). A wave amplitude was normal (Table 2).

Right-side Doppler (Fig. 1). The onset of transtricuspid flow was strikingly delayed with respect to P2 by 160 ms compared to only 40 ms in normals (p < 0.001). E-wave acceleration time was shorter than normal by 25 ms (p < 0.001), and peak E-wave velocity was reduced (p < 0.001), although mean acceleration rate was within the normal range. On the other

Table 2. Right Ventricular and Septal Long Axis Function

	Controls (n = 2)	Patients (n = 17)	
		Pre ACE-I	With ACE-I
Total excursion (cm)	2.6 ± 0.3	1.6 ± 0.5**	1.7 ± 0.6§
Peak shortening rate (cm/s)	10 ± 2.0	7.3 ± 2.5**	7.5 ± 2.9‡
Dimension change during IVRT (mm)	3 ± 1	7 ± 2*	3 ± 1.2†
Peak lengthening rate (cm/s)	10 ± 2.5	6.3 ± 2.3**	5.9 ± 3.6‡
P2-peak lengthening (ms)	150 ± 7	92 ± 4**	100 ± 6§
A wave amplitude (cm)	0.9 ± 0.1	0.78 ± 0.3	0.84 ± 0.3

*p < 0.01; **p < 0.001 patients before ACE-I vs. controls (unpaired *t* test); †p < 0.01 patients with ACE-I vs. before ACE-I (paired *t* test); ‡p < 0.01; §p < 0.001 patients after ACE-I vs. controls (unpaired *t* test). ACE-I = angiotensin-converting enzyme inhibition; IVRT = isovolumic relaxation time.

Table 3. Right Ventricular Inflow and Outflow Values

	Control (n = 21)	Patients (n = 17)	
		Pre-ACE-I	With ACE-I
Tricuspid Doppler			
P2-onset of flow (ms)	40 ± 15	160 ± 90**	75 ± 55§
Peak E wave velocity (cm/s)	40 ± 15	10 ± 14**	29 ± 10§
E acceleration time (ms)	80 ± 23	54 ± 11**	83 ± 25
E acceleration rate (m/s ⁻²)	5 ± 1	5.6 ± 2.7	4 ± 1
Early diastolic pressure gradient (mm Hg/cm)	0.38 ± 0.08	0.4 ± 0.1	0.28 ± 0.1‡
E deceleration time (ms)	140 ± 20	77 ± 14**	93 ± 31§¶
E deceleration rate (m/s ⁻²)	3.0 ± 0.8	3.9 ± 1.5*	3.6 ± 1.0
Peak A wave velocity (cm/s)	20 ± 10	39 ± 20*	30 ± 13
E/A ratio	1.9 ± 0.4	0.47 ± 0.8**	1.2 ± 0.7§
Total filling time (ms)	385 ± 150	170 ± 60**	320 ± 100§
Total diastolic time (ms)	460 ± 20	335 ± 90**	410 ± 50‡
Filling/diastolic time (%)	95 ± 8	50 ± 12**	80 ± 13§
PV-RA pressure drop (mm Hg)	—	45 ± 6	30 ± 5§
P2-end of TR (ms)	—	43 ± 5	29 ± 2.5†
Peak pulmonary velocity (cm/s)	75 ± 10	63 ± 20	70 ± 20†
Pulmonary ejection time (ms)	325 ± 25	235 ± 31**	240 ± 25¶
Pulmonary stroke distance (cm·s ⁻²)	11.8 ± 2.0	7 ± 2.4**	9.3 ± 2.9

*p < 0.01; **p < 0.001 patients before ACE-I vs. controls (unpaired *t* test); †p < 0.01; ‡p < 0.005; §p < 0.001 patients with ACE-I vs. before ACE-I (paired *t* test); ||p < 0.01; ¶p < 0.001 patients after ACE-I vs. controls (unpaired *t* test). ACE-I = angiotensin-converting enzyme inhibition; RV-RA = right ventricular-right atrial; TR = tricuspid regurgitation.

hand, E wave deceleration time was 50% less than normal, so that mean deceleration rate was higher ($p < 0.01$). Peak A wave velocity was 19 cm/s higher than normal ($p < 0.001$). Thus, E/A ratio was only one fourth the normal value in patients ($p < 0.001$). The delayed onset of flow caused total RV filling time to be less than 50% that in normals whether expressed in absolute terms or as a percentage of total diastole ($p < 0.001$ each). The mean systolic pressure drop between the right ventricle and the right atrium, as assessed from the tricuspid regurgitation, was 46 mm Hg. Peak pulmonary artery ejection time and systolic stroke distance were both lower than normal ($p < 0.001$) (Table 3).

With ACE-I (Tables 1 to 3). *Left ventricle.* With the start of ACE-I, LV cavity dimensions both fell but fractional shortening did not change. The delay in the onset of transmitral flow with respect to A2 increased by 120 ms ($p < 0.001$). E wave deceleration time increased and both mean acceleration and deceleration rates dropped strikingly, as did early diastolic pressure gradient compared with pre-ACE-I values ($p < 0.001$). E-wave velocity fell and that of the A wave increased so that E/A ratio fell to one third of control value. Total transmitral flow period did not change, although diastole itself increased by 60 ms, but the ratio between the two showed no consistent change after ACE-I (Table 1).

On the right side (Fig. 1). The RV-RA peak systolic pressure drop fell by 15 mm Hg, although all aspects of systolic long axis function (total excursion, peak shortening rate and time interval between q wave and peak shortening rate) were unaltered (Tables 2 and 3). However, there were major changes in transtricuspid flow velocities. The onset of the E

wave occurred 85 ms earlier with respect to P2, peak E wave velocity more than doubled; deceleration time was prolonged but neither mean acceleration rate nor deceleration rate changed. Peak A wave velocity was also unchanged, so that E/A ratio doubled. The shortening of the time interval P2 to the onset of tricuspid flow meant that the extent of long axis lengthening before the onset of flow fell, but peak long axis lengthening rate itself was unchanged, as was the timing of the peak value that remained earlier than normal with respect to P2. Total tricuspid flow period more than doubled, although diastolic time itself increased only by 20% so that there was a marked increase in the ratio of flow time to total diastolic time ($p < 0.001$). Peak pulmonary artery velocity also increased (Table 3).

Discussion

Findings. Our patients were selected to have systolic LV disease with a restrictive filling pattern. The left-sided changes with ACE-I were explicable on the basis of a reduction in left atrial (LA) pressure rather than any direct cardiac effect (5). On the right side of the heart, the systolic pressure drop across the tricuspid valve under control conditions was 46 mm Hg, compatible with raised LA and pulmonary artery pressures. The amplitude of RV, long axis motion was reduced, along with both shortening and lengthening rates. Peak lengthening rate occurred early with respect to P2, but the extent of change in long axis with RA systole was normal. In spite of this, the major disturbances to the pattern of transtricuspid flow previously described were present (3). Peak E wave velocity was

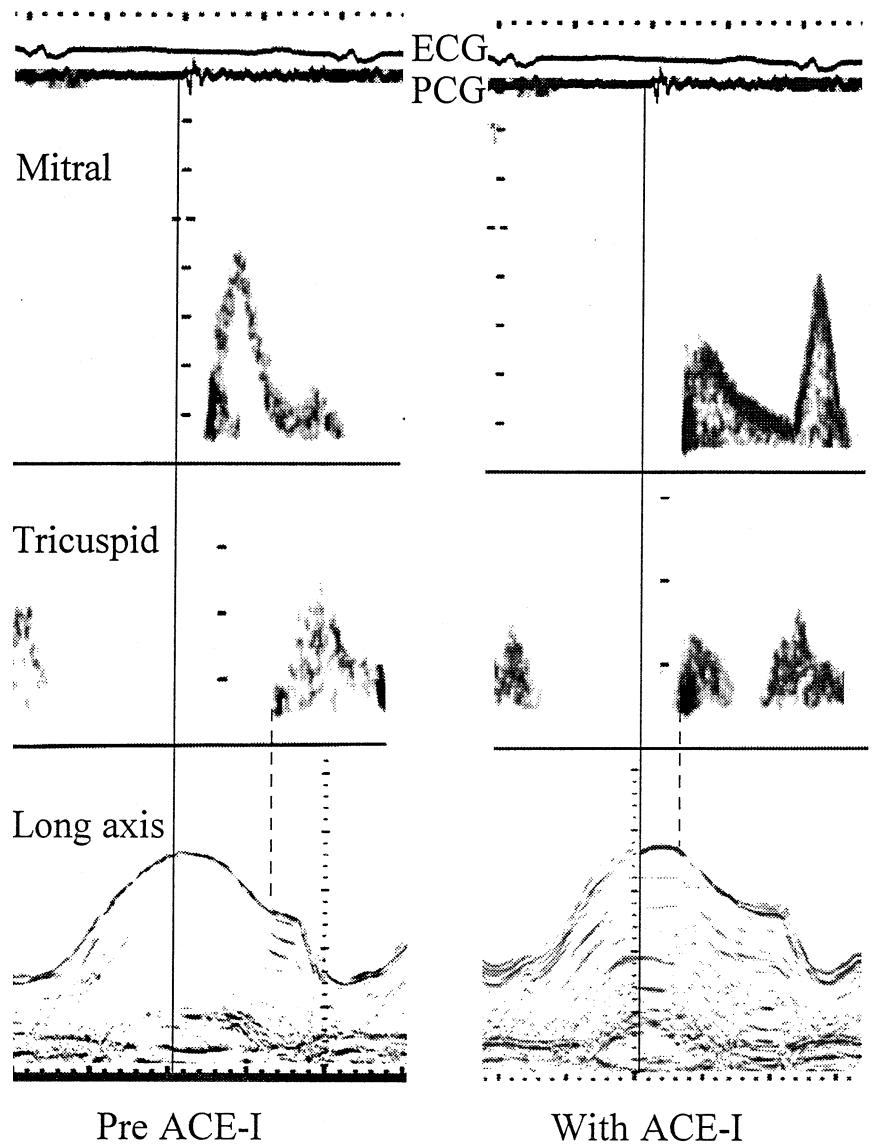


Figure 1. A composite of the transmittal and transtricuspid pulsed-Doppler flow and RV, long axis from a patient before ACE-I (left) and with ACE-I (right). Note the restrictive mitral filling pattern before treatment and its regression with ACE-I. There is no significant change in RV long axis motion with treatment, but tricuspid flow starts earlier and the extent of incoordinate RV ring motion falls. **Continuous vertical lines** represent A2 and **dotted vertical lines** represent the onset of tricuspid flow. Calibration: velocity 20 cm·s⁻¹; depth 1 cm; time 40 and 200 ms, respectively.

reduced, although mean acceleration and deceleration rates were both normal. The onset of detectable flow across the valve in early diastole was strikingly delayed by a mean value of 160 ms; during this period, 44% of total long axis lengthening had occurred, implying incoordinate filling (2). As a result of this delay, the total period of transtricuspid flow was reduced to 170 ms, representing only 50% of the total diastolic period, compared with a value of 83% of the left. A wave amplitude was somewhat increased so that E/A ratio was low. The nature of the right-side abnormalities thus differed fundamentally from those on the left.

Right-side events also changed strikingly with ACE-I. As would be expected from a fall in LA pressure, the systolic pressure drop across the tricuspid valve fell by 15 mm Hg. In spite of this, the dynamics of right-side long axis did not change. The main changes were in the pattern of transtricuspid flow. The onset became earlier, and its overall duration increased by over 100 ms,

so that it came to occupy 80% of the total diastolic time. E wave amplitude increased, but neither mean acceleration rate nor local pressure gradient changed. A wave amplitude was unaltered, but E/A ratio increased. ACE-I thus led to a normalization of RV filling, the changes being largely in the opposite direction to those occurring on the left side.

Mechanisms. There are a number of possible mechanisms for these right-side abnormalities. In any population of patients with LV disease, additional involvement of the right ventricle by the same or a related disease process will be present to a variable extent in individual patients (6). In addition, the right heart is subject to abnormal loading conditions caused by elevation of the LA pressure transmitted via the pulmonary artery and also of RA pressure (7). A low stroke volume may be imposed on it by severe left-side disease. Finally, the right side is subject to ventricular interaction mediated either via the pericardium or the septum (8-10).

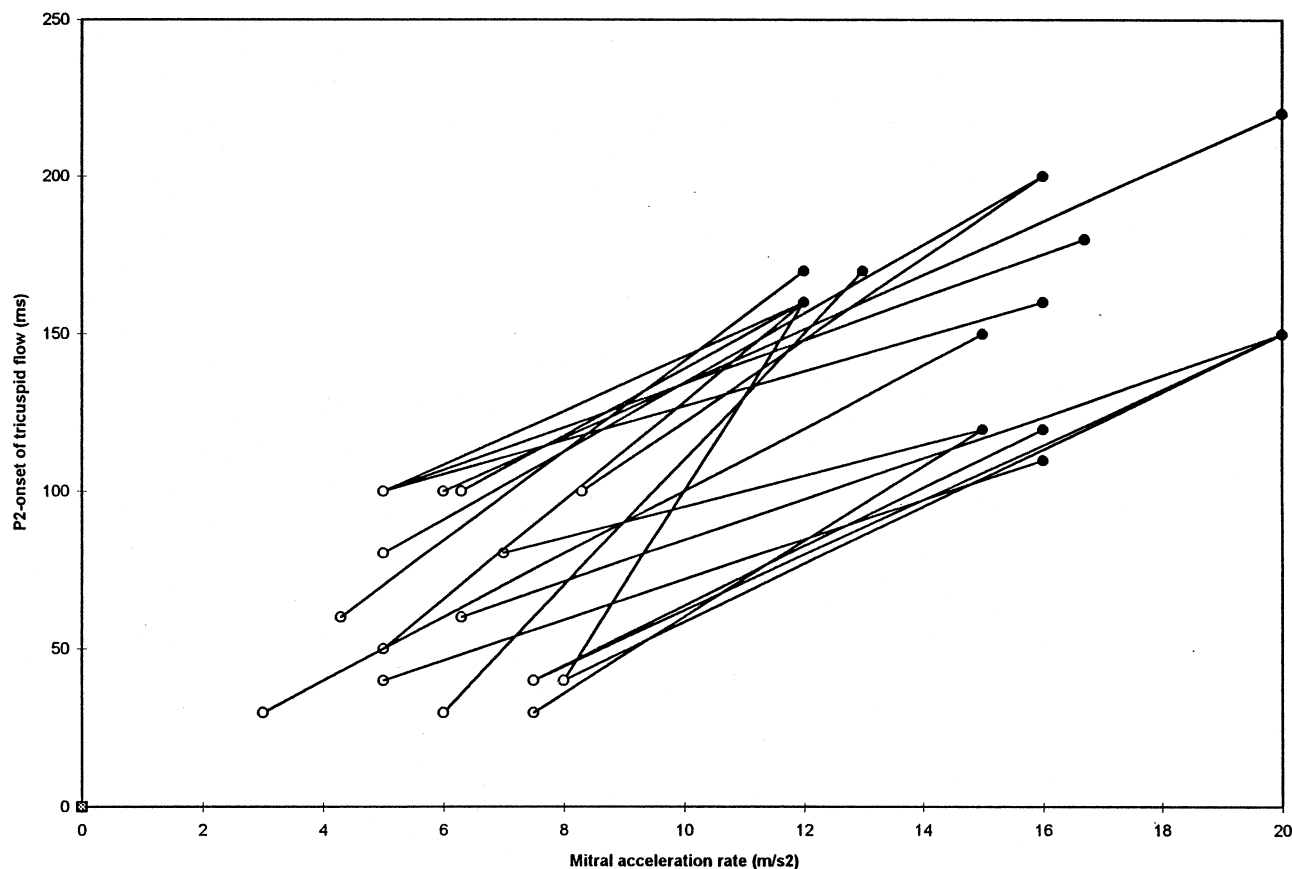


Figure 2. A plot in individual patients of transmitral E wave acceleration rate versus the time interval between P2 and the onset of tricuspid flow. Note the consistent fall of the former coinciding with shortening in the latter in all patients. **Closed circles** = patients under control condition; **open circles** = after treatment.

Some of these possible mechanisms were seen in the present series of patients. The peak systolic pressure drop supporting tricuspid regurgitation was increased under control conditions and fell with treatment. The reduced extent of RV, long axis shortening is compatible with additional RV disease rather than abnormal loading because neither its extent nor its velocity was affected as RV to pulmonary artery pressure difference fell.

The most striking abnormality under control conditions was in the timing of tricuspid flow so that its onset was more than 100 ms later than normal, leading to marked asynchrony when compared to early diastolic lengthening of the RV long axis. Neither the timing nor the velocity of this lengthening was affected by ACE-I, making a primary disturbance of RV relaxation a very unlikely cause. As the timing of flow reverted toward normal, the extent of asynchrony regressed. Once the transtricuspid E wave pressure gradient developed, it was normal under control conditions, and was slightly affected by treatment. A change in the magnitude of the pressure gradient therefore was not the cause of abnormal flow. An increase in peak tricuspid regurgitation pressure is always accompanied by

prolongation of overall RV systole by approximately 10 ms for each 10 mm Hg peak pressure increase (11). This effect was demonstrated with ACE-I in our patients with a fall in the interval from P2 to the end of regurgitation by 15 ms, but it was much too small to explain the change in the timing of flow, thus excluding another possible mechanism. There was a striking return of the timing of transtricuspid flow towards normal, however, as the restrictive filling pattern on the left side of the heart resolved by treatment. This was apparent not only from group values but from those in individual patients (Fig. 2). It occurred as the left-side pressure gradient fell from supranormal values before treatment to abnormally low volumes afterward. It seems, therefore, that the likeliest explanation for our findings is an early diastolic ventricular interaction and we hypothesize that high left-side pressures may delay the onset of a forward pressure gradient and hence atrioventricular diastolic flow on the right side.

Limitations. The most significant limitation is that the findings apply only to patients taking diuretics in clinically appropriate doses, which will certainly have modified right-side atrioventricular pressure gradients. Indeed, this is a major indication for their use. Unfortunately, it is effectively impossible in the West to recruit patients with heart failure who have not already been treated with diuretics (12). We did not attempt to measure pressure gradients directly. Unlike simple pressures, measuring pressure gradients, which have the physical dimensions of $\text{mm Hg}\cdot\text{cm}^{-1}$, requires at least two high-

fidelity catheter transducers across the valve with their sensitive elements a certain distance apart. Such records are technically difficult to make and are seldom undertaken. Instead, we preferred to rely on the relationship between force and acceleration as defined by Newton's Second Law of Motion to calculate the pressure gradient from the more easily measured velocity. Theoretically, Doppler signals may be delayed with respect to echocardiographic data resulting from fast Fourier transform algorithm. We have previously shown them to be small (13). Their presence would not affect estimates of overall filling time nor relative changes associated with treatment. As in previous studies, partial merging of E and A waves means that deceleration time has to be measured by extrapolation, and apparent a wave amplitude may be sensitive to heart rate, although it did not significantly change with ACE-I. When investigating ventricular interactions, measurements should ideally be made on both sides of the heart simultaneously, particularly when the timing of events is being correlated. Unfortunately, this is not possible with standard echocardiographic equipment. Finally, with the relatively small number of patients studied, it was not possible to investigate any possible correlation of these disturbances with underlying diagnoses.

Conclusions. Our results indicate that a restrictive filling pattern of the left side of the heart is often associated with striking delay in the onset of transtricuspid flow on the right side, with secondary incoordination and reduction in peak E-wave velocity. Right ventricular disease or a primary disturbance of RV relaxation are unlikely causes. Their regression along with that of the restrictive filling pattern on the left side with ACE-I strongly suggests that right-side filling abnormalities may be directly related to high early diastolic pressures in the left ventricle. The time relations between the two within the cardiac cycle seem to indicate a direct ventricular interaction rather than the simple effect of secondary pulmonary hypertension. We suggest that the implications of these right-side abnormalities merit further study, particularly with respect to their relation to fluid retention, exercise tolerance and heart

rate variability. Their prompt regression with ACE-I provides further evidence of the comprehensive effects of these remarkable drugs.

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