Acute Changes of Left Atrial Distensibility in Congestive Heart Failure

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Summary

Background: Investigations of the left atrial (LA) distensibility have revealed that it plays a major role in atrial function; however, LA distensibility has not as yet been studied in congestive heart failure (CHF).

Hypothesis: The study was undertaken to determine the effects of acute administration of esmolol, isosorbide dinitrate, dobutamine, and normal saline infusion on LA dimension, pressure, and distensibility.

Methods: The study included 23 patients with CHF (18 with ischemic heart disease and 5 with idiopathic dilated cardiomyopathy). Left atrial diameters (D) and pressures (P) were recorded at rest and thereafter during acute tests. P and D data during the ascending limb of the V loop were fitted to the exponential function $P = b \cdot e^{aD}$, where a is the passive elastic chamber stiffness constant and b is the elastic constant. The instantaneous diastolic LA distensibility (IDLAD) was calculated as $1/(dP/dD) = 1/a \cdot P$.

Results: The constant, a , increased significantly after normal saline and esmolol infusion ($p < 0.001$), while it significantly decreased after isosorbide dinitrate ($p < 0.001$) and dobutamine administration ($p < 0.05$) compared with baseline. Instantaneous diastolic LA distensibility (in mm/Hg) was 0.16 at baseline; it significantly increased after isosorbide dinitrate (0.32) and dobutamine (0.24) administration, while it significantly decreased after normal saline (0.11) and esmolol (0.12) infusion ($p < 0.001$ for all).

Conclusion: In CHF, LA distensibility may acutely increase with vasodilators or inotropics or may decrease with beta blockade or volume loading.

Key words: heart failure, atrial distensibility, esmolol, pressure–diameter relation

Introduction

The atrial function as a volume reservoir of blood during ventricular systole, a passive conduit of blood during early ventricular diastole, and a contractile chamber during late ventricular diastole has been studied extensively.^{1–3} Investigations of distensibility have revealed that it plays a major role in atrial function. Increased left atrial (LA) distensibility may benefit cardiac hemodynamics, ultimately increasing cardiac output⁴ through augmented LA reservoir function.⁵ It has been reported that increased LA distensibility prevents a rise in LA pressure.⁶ The LA appendage is more distensible than the body of the left atrium in vivo.⁷ When left ventricular filling pressure is increased and global atrial distensibility is decreased,⁸ improved distensibility of the appendage rather than of the body of the LA may be beneficial. Data regarding changes in atrial distensibility during atrial fibrillation are ambiguous and contradictory.^{9–11} In atrial fibrillation, atrial systole is absent, and usually a rapid and irregular ventricular rate is induced. Cardiac output declines after atrial fibrillation induction^{12, 13} because of the loss of the atrial booster pump function. However, in patients with sinus rhythm and heart failure, LA function often plays a critical role.

We investigated LA chamber stiffness and its influence on cardiac performance in patients with congestive heart failure (CHF) using LA pressure–diameter analysis and LA distensibility changes in different loading conditions induced by esmolol, dobutamine, and isosorbide dinitrate administration, and by normal saline infusion.

Methods

Patients

We studied 23 patients with congestive heart failure (CHF) in New York Heart Association (NYHA) class III. In 18 of these patients, cardiac catheterization showed ischemic cardiomyopathy and 5 patients had idiopathic dilated car-

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diomyopathy. Sinus rhythm was present in all patients without atrioventricular or intraventricular conduction disturbances. Patients with coexisting significant valve disease were not included.

Cardiac Catheterization and Echocardiography

All medications were discontinued for five half-lives before catheterization. After informed consent was obtained, diazepam (5 mg) was given orally 1 h before the study. A Swan-Ganz catheter 7F was placed in the pulmonary artery through the right femoral vein. All pressures were referenced to 50% of the transthoracic diameter and were obtained at end tidal volume apnea. They were recorded on a physiologic recorder (Mennen-Horizon-2000, Mennen Medical, Inc., Clarence, N.Y.), and the pressure signals were electronically transmitted to the auxiliary input of a Hewlett-Packard Sonos 1000 (Hewlett-Packard Company, Andover, Mass.) echocardiographic device so that simultaneous recordings of pressure, M-mode echocardiogram, and electrocardiogram were obtained (Fig. 1). All data were recorded on a videocassette recorder for later playback and analysis.

Left atrial pressure was measured by pulmonary capillary wedge pressure (PCWP). Left atrial M-mode echocardiography was carried out by directing the M-mode echo beam to the aortic root where the LA dimension was obtained. Recordings were obtained when all hemodynamic parameters were stable.

After baseline measurements were taken, intravenous esmolol hydrochloride administered in a bolus dose of 500 $\mu\text{g/kg/min}$ and in continuous infusion of 50 $\mu\text{g/kg/min}$ sufficient to decrease heart rate by 15%. When hemodynamic values were stabilized, repeat echocardiogram and hemodynamic measurements were obtained. Ten min later, the esmolol

infusion was discontinued and the hemodynamic values were allowed to return to baseline. After 30 min, sublingual isosorbide dinitrate was administered to decrease peak systolic blood pressure by 10 mmHg, followed by repeat echocardiographic and hemodynamic measurements. Three h later, the hemodynamic values returned to baseline again and intravenous dobutamine was infused at a rate of 2.5–10 $\mu\text{g/kg/min}$ sufficient to increase heart rate by 15%, followed by repeat echocardiographic and hemodynamic measurements. After hemodynamic values returned to baseline once more following the discontinuation of dobutamine, 300–800 ml of normal saline was rapidly infused to increase wedge pressure by 30% above the baseline. Subsequent repeat hemodynamic and echocardiographic measurements were done.

Data Analysis—Calculation of Atrial Distensibility

Of the recorded tracings, frame by frame LA diameters were measured manually, and the LA time/diameter curve was plotted using the *Excel for Windows* computer program. The LA pressure–diameter loop was obtained from the LA time–diameter curve and the real-time LA pressure curve (Fig. 2). The LA pressure/dimension relation was composed of two loops (Fig. 3): the A loop expressing the pump function of the LA, and the V loop expressing the LA reservoir function. Left atrial pressure/diameter data obtained during the atrial filling phase, which corresponds to the ascending limb of the V loop from the nadir of the X wave of LA pressure to the peak of the V wave, were used for the calculation of LA diastolic distensibility⁵ (Fig. 3). Pressure and diameter data during the ascending limb of the V loop were then fitted to the exponential function, $P = bxe^{ad}$. The least-squares method was used for calculation of a and b , where a is the passive elastic chamber stiffness constant (mm^{-1}) which determines the slope of the exponential curve,^{5,6} and b is the elastic constant (mmHg). The instantaneous atrial diastolic distensibility was calculated as $1/(dP/dD) = 1/a \cdot P$, where P is the atrial pressure recorded the peak of the V wave. Left atrial distensibility was calculated at baseline and in the pharmacologic tests.

FIG. 1 Simultaneous record of M-mode echocardiogram, electrocardiogram, and pulmonary capillary wedge pressure.

FIG. 2 Left atrial pressure and left atrial diameter drawn by the *Excel for Windows* computer program.

FIG. 3 The left atrial pressure-diameter loop is made up of an A loop representing left atrial systolic function and a V loop representing left atrial reservoir function. Left atrial pressures and diameters during the ascending limb of V loop and calculated monoexponential curve are shown.

Statistics

Changes in atrial diameter, pressure, and distensibility from the control state to each interventional state were compared using Student's paired *t*-test. A probability (*p*) value of <0.05 was considered significant.

Results

Baseline Characteristics

In all, 16 men and 7 women (mean age 62.3 years) were studied. Left ventricular resting ejection fraction was 32%. Baseline characteristics are shown in Table I.

TABLE I Baseline characteristics

Characteristics	Patients (n = 23)
Clinical parameters	
Age (years)	62.3 ± 6.5
Sex (M/F)	16/7
Body surface area (m ²)	1.72 ± 0.24
Systolic blood pressure (mmHg)	125 ± 13
Diastolic blood pressure (mmHg)	82 ± 10
Heart rate (beats/min)	87 ± 9
Congestive heart failure	
Duration of symptoms (months)	16 ± 3
Idiopathic/ischemic	5/18
Remote myocardial infarction	15/18
By-pass surgery	8/18
NYHA class	III
Ejection fraction (%)	32 ± 4
Treatment	
Digitalis	18
Diuretics	22
ACE inhibitors	21
Nitrates	16

Abbreviations: M = male, F = female, NYHA = New York Heart Association, ACE = angiotensin-converting enzyme.

Hemodynamic Effects of Drug Administration

Following pharmacologic interventions there were significant changes in hemodynamic and echocardiographic parameters which are shown in Table II.

Left Atrial Stiffness

The LA pressure/diameter relation during the atrial filling phase fitted the exponential function closely. The correlation coefficient *r* was 0.92 (0.84–0.99) (Fig. 3).

TABLE II Effect of drug administration on hemodynamic and echocardiographic parameters

	Baseline	Esmolol	Normal saline	ISDN	Dobutamine
HR (beats/min)	87 ± 9	74 ± 8 ^c	90 ± 10	86 ± 10	100 ± 12 ^c
SBP (mmHg)	125 ± 13	115 ± 12 ^a	134 ± 14	110 ± 12 ^c	135 ± 15 ^a
DBP (mmHg)	82 ± 10	74 ± 9 ^b	95 ± 11 ^c	70 ± 8 ^c	93 ± 10 ^c
EF (%)	32 ± 4	31 ± 4	34 ± 4	40 ± 6 ^c	42 ± 6 ^c
SV (ml)	50 ± 6	47 ± 5	59 ± 6	64 ± 7	68 ± 7
PCWP (mmHg)	18 ± 2.5	20 ± 3 ^a	23.5 ± 3.5 ^c	12.5 ± 3.7 ^c	16.1 ± 2.1 ^b
a (mmHg)	22.7 ± 3.4	24 ± 2.5	28 ± 3.4 ^c	15 ± 2.1 ^c	20 ± 3.7 ^a
v (mmHg)	32.5 ± 4.5	33 ± 4.6	35 ± 5.1	20 ± 3.8 ^c	25 ± 2.9 ^c
x (mmHg)	10.9 ± 2.5	12 ± 2.3	16 ± 2.8 ^c	6.3 ± 1.4 ^c	10 ± 1.9
y (mmHg)	14.1 ± 2.5	16.5 ± 2.8 ^c	19 ± 3.2 ^c	7.5 ± 1.3 ^c	13 ± 2.6
d _{max}	45 ± 4.3	44.8 ± 4.5	45.4 ± 4.8	42.7 ± 4.3	44.6 ± 4.6
d _a	42 ± 4.4	43 ± 4.2	44.8 ± 4.5 ^a	40.8 ± 4.1	41.6 ± 4.2
d _{min}	38.5 ± 3.8	39.3 ± 3.9	41.6 ± 4.2 ^a	36.7 ± 3.5	37.9 ± 4.2

^a*p*<0.05, ^b*p*<0.01, ^c*p*<0.001 comparison between pharmacologic interventions and baseline using paired *t*-test.
Abbreviations: ISDN = isosorbide dinitrate; HR = heart rate; SBP and DBP = systolic and diastolic blood pressure; EF = left ventricular ejection fraction; SV = left ventricular stroke volume; PCWP = pulmonary capillary wedge pressure; a, v, x, y = pulmonary capillary wedge pressure during a, v, x, y waves, respectively; d_{max}, d_a, d_{min} = maximal, at the P wave of electrocardiogram and minimal left atrial diameter.

Compared with baseline, LA chamber stiffness constant was significantly greater after esmolol administration and normal saline infusion ($p < 0.001$), while it was significantly decreased after dobutamine ($p < 0.001$) and after isosorbide dinitrate administration ($p < 0.05$, Table III).

Instantaneous atrial diastolic distensibility was 0.16 mm/mmHg at baseline when atrial pressure levels P_v were 32.5 mmHg (P_v : peak of the V wave). It increased after sublingual isosorbide dinitrate (0.32 mm/mmHg, at a lower P_v (20 mmHg, $p < 0.001$) and after dobutamine (0.24 mm/mmHg, $p < 0.001$) at a lower P_v (25 mmHg, $p < 0.001$). It decreased after normal saline infusion (0.11 mm/mmHg, $p < 0.001$) at a similar P_v (35 mmHg, $p = \text{NS}$) and after esmolol (0.12 mm/mmHg, $p < 0.001$) at a similar P_v (33 mmHg, $p = \text{NS}$), (Table III).

Discussion

The left atrium is positioned at the inlet to the left ventricle and functions as a reservoir for blood returning from the pulmonary vein during left ventricular systole. In addition, the left atrium acts as conduit during early and mid-diastole, when blood is transferred from the pulmonary veins to the ventricles. During atrial systole, this chamber acts as a booster pump enhancing ventricular end-diastolic filling.

In congestive heart failure, the LA pressure/diameter loop is made up of an a loop representing LA systolic function and a V loop which represents LA reservoir function. Left atrial chamber stiffness is obtained by fitting the LA pressure/diameter relation in the ascending limb of the V loop to an exponential function. The LA chamber stiffness constant tended to be greater after normal saline infusion and esmolol administration, while it decreased after sublingual isosorbide dinitrate and dobutamine infusion.

Increased LA chamber stiffness can be caused by an increase in LA muscle stiffness.¹⁴ A part of LA stiffness increase may be attributable to LA myocardial function changes caused by increased LA afterload.¹⁵ Another possibility may be the increase of intracellular calcium concentration in the atrial fibers reported to augment LA stiffness.^{16, 17}

A negative correlation of LA chamber stiffness to LA reservoir dimension was observed in this study. Thus, in these patients with CHF, LA reservoir function is reduced by the increase in LA chamber stiffness. In this way, LA stiffness may primarily affect left ventricular filling.

The importance of LA reservoir function was emphasized by Grant *et al.*, who estimated that 42% of the left ventricular stroke volume (and its associated energy) is stored in the left atrium during left ventricular systole.² Thus, isosorbide dinitrate and dobutamine administrations may contribute significantly to left ventricular filling in CHF increasing LA distensibility and atrial systolic function. Moreover, Suga⁴ reported a decrease in stroke volume when atrial distensibility was reduced, even though atrial pressure was allowed to increase.

In the calculation of atrial distensibility, we used atrial diameter rather than volume. At present, there is no technique available to measure precisely instantaneous atrial volume,

TABLE III Changes in left atrial distensibility

	Stiffness (mm ⁻¹)	Distensibility (mm/mmHg)
Baseline	0.20 ± 0.05	0.16 ± 0.03
Esmolol	0.27 ± 0.04 ^b	0.12 ± 0.02 ^b
Normal saline	0.25 ± 0.03 ^b	0.11 ± 0.02 ^b
Isosorbide dinitrate	0.16 ± 0.03 ^b	0.32 ± 0.04 ^b
Dobutamine	0.17 ± 0.04 ^a	0.24 ± 0.04 ^b

^a $p < 0.05$, ^b $p < 0.001$ comparison between pharmacologic interventions and baseline using paired *t*-test.

mainly because of the complexity of atrial geometry. On the other hand, good correlations between LA anteroposterior minor axis and atrial volume have been reported.^{18, 19} Thomas *et al.*²⁰ reported that a selective reduction of atrial distensibility leads to a concomitant increase in atrial pressure. In the intact circulation, however, redistribution of blood toward the central circulation might occur. This could be the result of a decrease in cardiac output with a concomitant reduction in arterial pressure and a baroreflex-induced displacement of blood from the splanchnic region.²¹ Hence, changes in atrial pressure do not necessarily reflect changes in atrial distensibility. Left atrial pressure, was derived from PCWP. Although PCWP is widely used to evaluate LA pressure, it may not be as precise as has been assumed.²² However, this limitation was counterbalanced by the fact that the study patients served as their own controls, while methodology was identical in all measurements.

Conclusion

In congestive heart failure, ventricular filling is primarily affected by atrial function, which depends on atrial distensibility, which may increase acutely with inotropics or nitrates or decrease with volume loading or beta blockade. The clinical implications are obvious in acute failure, while the significance of chronic therapy on LA distensibility and overall hemodynamic conditions should be assessed in follow-up studies.

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