Effect of dynamic exercise on left atrial function in conscious dogs

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1. Dynamic changes in left atrial (LA) function during treadmill exercise were studied in ten conscious dogs instrumented to measure left ventricular (LV) pressure and diameter, LA pressure and diameter, and pulmonary venous blood flow (PVF, transit time flowmeter).
2. Systolic PVF volume (reservoir volume; a measure of LA reservoir function) increased from 38 ± 4% of total PVF volume at baseline to 52 ± 8% of total PVF volume during exercise, and diastolic PVF volume (conduit volume; a measure of LA conduit function) decreased from 62 ± 5% at baseline to 48 ± 8% during exercise ($P < 0.005$).
3. The increases in reservoir volume and the decrease in conduit volume were due not only to a greater decrease in diastolic interval than systolic interval but were also caused by a significantly greater increase ($P < 0.05$) in the mean systolic filling rate (93%) than in the mean diastolic filling rate (51%).
4. During exercise the pattern of LV filling derived from changes in LV diameter showed that a greater percentage of LV filling occurred during the second half of diastole at the time of atrial contraction ($P < 0.05$), suggesting that LA booster function was enhanced.
5. Changes in LA dimension revealed that during exercise more blood volume was reserved in the LA during systole and that this change was associated with an increase in the LA dimension at the beginning of LA contraction ($r = 0.61$, $P < 0.05$).
6. We conclude that LA reservoir and booster functions were augmented during exercise, whereas conduit function was not. Increased reservoir function may play an important role in accelerating LV filling by helping to maintain an enhanced atrioventricular pressure gradient during diastole and also by increasing LA booster function through an increase in LA preload.

The mechanical characteristics of the left ventricle (LV) have been the subject of extensive study because of the obvious importance of that chamber in pumping blood through the systemic circulation. In contrast, left atrial (LA) function is poorly understood despite its key role in optimizing LV diastolic function. The LA functions not only as a conduit but also as a booster pump for augmentation of LV filling and as a reservoir for storing blood during ventricular systole (Grant, Bunnell & Greene, 1964; Payne, Stone & Engelken, 1971). It has been proposed that augmented LA booster function is one of the mechanisms compensating for decreased early filling in patients with decreased LV compliance (Benchimol, Ellis & Dimond, 1965; Rahimtoola, Ehsani, Sinno, Loeb, Rosen & Gunnar, 1975). Although some reports suggest that there is an inverse relationship between ventricular systolic function and the relative importance of atrial booster function (Benchimol *et al.* 1965; Rahimtoola *et al.* 1975), little is known about changes in conduit and reservoir function of the LA during normal activity and in various disease states (Grant *et al.* 1964; Toma *et al.* 1989). One would expect that the three aspects of LA function might interact and vary to accommodate to changes in LV filling requirements. There have been no studies which describe the simultaneous changes in reservoir, transport and booster functions during exercise.

The cardiac response to exercise is complex and involves changes in heart rate, contractility, preload, and afterload. In intact, apparently normal, patients the relaxed LA is less compliant than the LV (Nagano *et al.* 1989),

thus facilitating passive transfer of blood between the two chambers during diastole. One could speculate that these passive properties of the thin-walled LA may be strongly influenced at higher volumes by the pericardium and surrounding tissues. Minor changes in LA pressure should have a considerable effect on the pattern of blood flow entering the LA from the pulmonary veins, since the pressure gradient between the pulmonary veins and the LA is normally very small. Thus, it is reasonable to expect that each of the functions of the LA may change during exercise. An understanding of the normal physiological response of the LA to exercise is important since abnormalities caused by disease processes may limit an individual's activity level. This study was undertaken to examine the effects of exercise on LA conduit, reservoir and booster functions in chronically instrumented dogs.

This study was presented in part at the annual scientific sessions of the American Heart Association (Nishikawa, Roberts, Tan & Klopfenstein, 1993).

METHODS

Surgical preparation

Ten adult mongrel dogs weighing 25–30 kg were selected for study. Each animal was brought to the laboratory, following an overnight fast, and anaesthetized, intubated and ventilated with a volume respirator (Model 607, Harvard Apparatus Co., Inc., Millis, MA, USA) and vaporizer (Fluotec, Cyprane Keighley Ltd, Keighley, UK) using 0·5–2·5% fluothane in oxygen. Arterial blood gases were monitored periodically. A left thoracotomy was performed aseptically in the fifth intercostal space and Tygon fluid-filled transvascular catheters were placed in the right atrium and descending thoracic aorta.

After a 3–4 cm longitudinal incision had been made in the pericardium, an ultrasonic transit time flowprobe (Transonics, Inc., Ithaca, NY, USA) was implanted around the ascending aorta, beyond the origin of the coronary vessels. A high-fidelity catheter-tipped micromanometer (Konigsberg Instruments, Pasadena, CA, USA) and a Tygon fluid-filled catheter for transducer calibration were inserted through the LV apex to measure LV pressure. A pair of ultrasonic dimension crystals (crystal material LTZ-2, Transducer Products, Goshen, CT, USA) were implanted on the endocardium of the LV to measure the anterior–posterior diameter (later referred to as the LV dimension). A second ultrasonic flowprobe (Transonics, Inc., 6 or 8 mm i.d.) was placed close to the LA around the largest accessible pulmonary vein. In preliminary studies we simultaneously measured blood flow in three pulmonary veins and found that changes in volumetric blood flow and blood flow waveforms varied in the same way in all of them. In seven animals a second micromanometer and catheter were inserted through the LA appendage to measure LA pressure, and another pair of ultrasonic crystals were implanted on the epicardial surfaces of the LA to measure the anterior–posterior diameter (LA dimension). The cut edges of the parietal pericardium were loosely sutured (in 7 animals), or closed with a continuous locking suture (in 3 animals). Intrathoracic leads were positioned for measurement of the electrocardiogram. All catheters and pressure transducer leads were passed individually through the chest wall and tunnelled subcutaneously to the back. A chest tube was positioned, the ribs were brought back together with umbilical tape, the wound was closed in layers to provide an airtight seal, and air was removed from the chest. The animals were kept warm and provided with supplementary oxygen and analgesia as needed during recovery from surgery. The pleural cavity was drained and all intravascular catheters were aspirated and refilled with a heparin solution daily. The three animals with closed pericardia had the volume of fluid in the pericardial space adjusted as often as needed via indwelling catheters to maintain separation of the visceral and parietal pericardia to prevent the formation of adhesions.

Experimental model

All animals were examined and cared for daily after surgery by the investigators as well as institutional veterinarians. The animals were standing, walking, eating and drinking normally by the second or third postoperative day. Starting 3 days after surgery, each animal was brought to the laboratory daily, or every other day, and allowed to stand in a sling. Data were examined to be sure that they were recovering properly from surgery and also to ensure that data quality was optimal. Animals were not exercised until haemodynamic values had stabilized in the normal range. We began to perform the experiments $10{\cdot}2 \pm 2{\cdot}1$ days after surgery. Before surgery animals were brought to the laboratory on several occasions and only those which demonstrated the ability and willingness to exercise on the treadmill were selected for surgery. All animals had elevated heart rates standing on the treadmill prior to exercise compared to those observed when they were resting in the sling, since they knew they would be exercising. The animals seemed to enjoy their excursions to the laboratory and the exercise periods.

Experimental protocol

Each conscious animal was brought to the laboratory and allowed to stand comfortably on the treadmill. After baseline data were recorded, the treadmill was started at 2 miles h^{-1} and kept at that rate for 2 min to let the animal get used to running on the treadmill. Then, the speed on the treadmill was increased to 3 miles h^{-1}, and finally 5 miles h^{-1}. Each of these stages was 3 min in length. Measurements were performed during the final 30 s of each stage. This procedure was repeated on several different days over a 1–2 week period so that each subject became comfortable with the protocol and the consistency of the data could be assured.

The animals were killed using 1 g I.V. sodium thiamylal followed by a 10 ml I.V. bolus of a saturated solution of potassium chloride. The positions of all catheters, transducers, and piezo-crystals were noted.

Data analysis

All signals were processed using a monitoring system developed in our laboratory which is based on a single signal conditioning module (1B31AN, Analog Devices, Norwood, MA, USA) and were recorded directly onto an IBM-compatible PC hard disk using the software package CODAS (DATAQ Instruments, Akron, OH, USA) at a sampling rate of 200 s^{-1}. All haemodynamic data were examined over a 30 s period at baseline and at each stage of exercise using a series of interactive programs developed in our laboratories (Tan, Vinten-Johansen & Klopfenstein, 1990). Each 30 s data file included several respiratory cycles, thus avoiding errors that

may have occurred from measuring subsets of single cycles. LV pressure and the LV anterior–posterior dimension were determined at end-diastole and end-systole. End-diastole was defined as occurring just before the beginning of the rapid upstroke in LV pressure. End-systole was defined as occurring 20 ms before the peak negative rate of change in LV pressure (dP/dt; Sasayama, Ross, Franklin, Bloor, Bishop & Dilley, 1976). The maximum rate of change of LV dimension ($dLVD/dt_{max}$) was determined and the time constant of the isovolumic LV pressure fall (T) was calculated using the Weiss method (Weiss, Fredericksen & Weisfeldt, 1976). T was used to provide an index of the rate of LV relaxation.

The analysis of left atrial function

In order to evaluate the three components of LA function, it is necessary to have indices of LA inflow (derived from pulmonary vein blood flow measurements), LA volume (LA anterior–posterior dimension was used), and LA outflow (indices of LV inflow were derived from LV dimensional measurements). The instantaneous changes in LV pressure, LV anterior–posterior diameter, LA pressure, LA anterior–posterior diameter, and pulmonary vein branch blood flow at baseline are shown in Fig. 1. These data were obtained when the animal was resting very quietly (its heart rate was 97 beats min^{-1}). The pulmonary vein blood flow (PVF) had two forward flow peaks: one during early systole, and the other in diastole during rapid filling of the LV. LA contraction produced a fleeting slowing or reversal of flow.

Because the mitral valve is closed during ventricular systole, all of the blood that enters from the pulmonary vein during systole is reserved in the LA. We used the volume of blood drained from the pulmonary vein and stored in the LA during systole as a measure of the reservoir function of the LA (reservoir volume, the dark-stippled area in Fig. 1, from end-diastole to the beginning of rapid filling of the left ventricle). The beginning of rapid filling was defined as the time when LA pressure first exceeded LV pressure. This reservoir function is also manifested by the changes in atrial diameter that occur during systole. LA diameter increases rapidly at the beginning of LV contraction and continues to increase throughout systole. The systolic peak of PVF was observed during LV isovolumic contraction in all of the animals. After mitral valve opening, the LA diameter begins to decrease, and at the same time PVF has its second forward peak. This atrial diameter shortening is not caused by active shortening of atrial muscle but by other means such as LV suction (passive atrial shortening) (Cheng, Freeman, Santamore, Constantinescu & Little, 1990). Although the atrial diameter increases slightly during the slow filling phase (suggesting that some reservoir function is transiently present), there is a net decrease in atrial diameter during diastole. Furthermore, when the heart rate is more rapid, as it was just prior to and during exercise in our animals, diastasis disappears and this increase in atrial diameter becomes less or is not present. Thus, in this preparation, the atrium acted mainly as an open conduit during diastole with blood flowing directly from the pulmonary vein through the mitral valve into the LV (conduit function) along with blood that had accumulated during systole (discharge of atrial capacitance). We defined conduit function as the volume of blood that passes from the pulmonary vein into the LA (conduit volume, the lightly stippled area in Fig. 1, from the beginning of rapid filling to end-diastole) during diastole. The analysis of conduit function used in this study is supported by previous reports (Morkin, Collins, Goldman & Fishman, 1956) of contrast material passing from the pulmonary vein directly through the LA

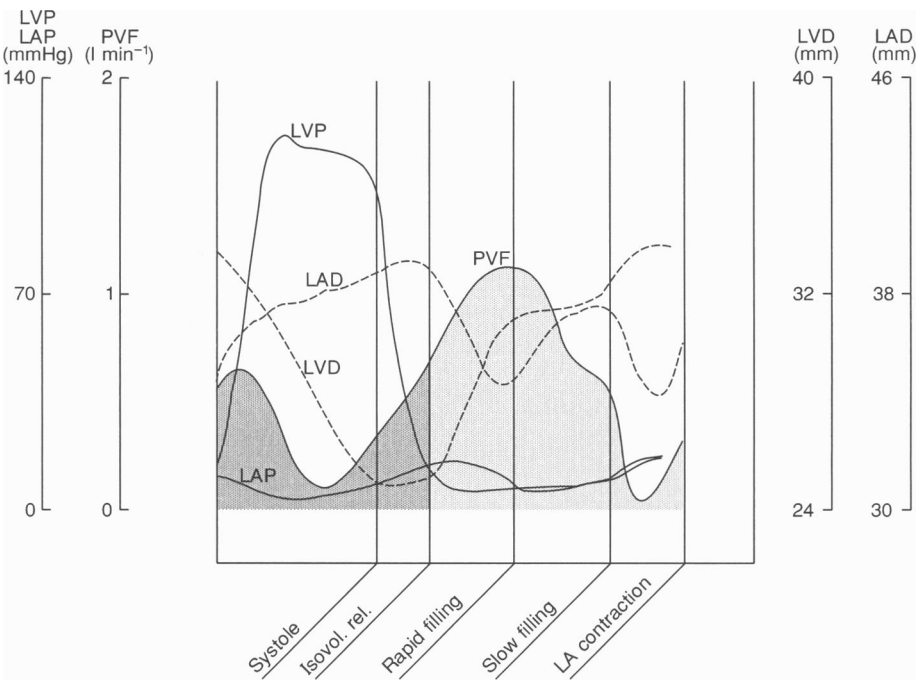

Figure 1

Simultaneous tracings of left ventricular blood pressure (LVP) and diameter (LVD), left atrial blood pressure (LAP) and diameter (LAD), and pulmonary venous blood flow (PVF) in a representative animal. Isovol. rel., Isovolumic relaxation.

into the LV. Finally, atrial contraction following the slow filling phase completed the filling of the left ventricle and resulted in a sharp increase in the left ventricular dimension (booster function). There is very little retrograde flow during LA contraction at baseline.

The PVF waveform was analysed to determine (1) the peak systolic and diastolic blood flow rate (reservoir peak flow rate and conduit peak flow rate, respectively) and the minimum flow rate during LA contraction, (2) the volume of blood flowing into the LA during ventricular systole (reservoir volume), and (3) the volume of blood that enters from the pulmonary vein and passes through the LA during diastole (conduit volume). To indicate the relative importance of reservoir and conduit functions in one beat, reservoir and conduit volumes were each expressed as a percentage of the total PVF recorded by the flowmeter. To be certain that the observed changes in reservoir volume and conduit volume were not simply caused by changes in the relative durations of systole and diastole as heart rate increased, the mean systolic and diastolic PVF rates (mean reservoir and conduit blood flow rates) were calculated as follows.

$$\text{Mean systolic PVF rate (ml min}^{-1}) = \frac{\text{reservoir volume}}{\text{systolic interval}}.$$

$$\text{Mean diastolic PVF rate (ml min}^{-1}) = \frac{\text{conduit volume}}{\text{diastolic interval}}.$$

The contribution of atrial contraction to LV filling was approximated as the increase in LV dimension during the second half of diastole expressed as a fraction of total (systolic) LV dimensional shortening. The LA diameter was differentiated with respect to time and the peak negative value of the first derivative when the LA diameter was decreasing during atrial contraction and the peak positive value when the LA diameter was increasing during LA relaxation were determined.

LA pressure was measured at the time of 'x-descent' (the time of peak systolic PVF), 'y-descent' (the time of peak diastolic PVF), and at the peak of the 'a-wave' (the atrial pressure wave caused by atrial contraction). The mean LA pressure during systole and during the whole cardiac cycle were also noted. The LA dimension was determined at (1) its maximum during systole, (2) its minimum during LA contraction, and (3) at the onset of LA contraction. In five of ten dogs, the onset of LA contraction was not discernible on the LA dimension tracings during exercise. In these animals the onset of LA contraction was considered to occur 65 and 55 ms before the end of diastole, during stage 1 and stage 2 respectively. These approximations were derived from the animals in which the onset of LA contraction was clearly observed (Fig. 2). The arrows mark the onset of LA contraction in each case and all tracings begin at end-diastole.

An increase in LA compliance during systole is associated with a greater accumulation of blood in the LA before mitral valve opening. In order to clarify the relationship between LA reservoir function and LA compliance, we calculated an index of the effective LA chamber compliance during ventricular systole as mean LA dimension divided by mean LA blood pressure before and during exercise.

Table 1. Effect of exercise on haemodynamic parameters

		Exercise	
	Baseline	Stage 1 (3 miles h^{-1})	Stage 2 (5 miles h^{-1})
Heart rate (beats min^{-1})	119 ± 14	168 ± 16*	193 ± 13*†
Mean aortic blood pressure (mmHg)	100 ± 11	110 ± 20	110 ± 18*
LVEDP (mmHg)	13·3 ± 4·2	11·9 ± 4·7	10·4 ± 4·4*†
Cardiac output (l min^{-1})	2·6 ± 0·6	3·8 ± 1·1*	4·4 ± 1·2*†
Stroke volume (ml)	20·1 ± 6·9	23·1 ± 6·9*	24·2 ± 6·9*†
LVEDD (mm)	35·4 ± 5·7	36·2 ± 5·6	36·3 ± 5·3
LVESD (mm)	28·3 ± 4·3	27·9 ± 4·3	27·0 ± 4·2*†
LV dP/dt_{max} (mmHg s^{-1})	2516 ± 637	3374 ± 690*	3871 ± 802*†
LV dP/dt_{min} (mmHg s^{-1})	−2622 ± 663	−3050 ± 690*	−3263 ± 563*†
Time constant (T)	28 ± 4·0	23 ± 2·8*	21 ± 2·7*†
$dLVD/dt_{max}$ (mm s^{-1})	105 ± 31	125 ± 27*	158 ± 37*†
ΔLV_{AB} dimension (mm)	3·3 ± 2·1	3·9 ± 2·1*	4·8 ± 2·1*†
Maximum LAD during systole (mm)	40·7 ± 2·5	42·3 ± 3·1*	43·0 ± 3·5*†
LAD at beginning of LA contraction (mm)	39·1 ± 3·1	40·2 ± 2·4	41·1 ± 2·6*†
Minimum LAD during LA contraction (mm)	36·9 ± 2·2	36·8 ± 2·5	37·1 ± 2·5
Mean LAP (mmHg)	7·6 ± 3·5	8·5 ± 4·0	8·6 ± 4·0
LAP at x-descent (mmHg)	4·9 ± 3·7	3·5 ± 4·8	3·0 ± 4·4*
LAP at y-descent (mmHg)	1·4 ± 3·1	1·5 ± 3·4	1·8 ± 3·6
Peak v-wave (mmHg)	10·6 ± 4·5	12·8 ± 4·6*	14·4 ± 4·2*†
Peak a-wave (mmHg)	13·7 ± 5·1	15·3 ± 3·7	14·4 ± 3·5
Effective LA compliance index (mm mmHg^{-1})	5·2 ± 0·4	6·6 ± 0·6*	6·4 ± 0·6*

LVEDP, left ventricular end-diastolic pressure; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; ΔLV_{AB} dimension, extent of shortening of LV apex–base dimension; LAD, left atrial dimension; LAP, left atrial pressure. *$P < 0·05$ *vs.* baseline. †$P < 0·05$ *vs.* stage 1. Greater degrees of statistical significance are noted in text.

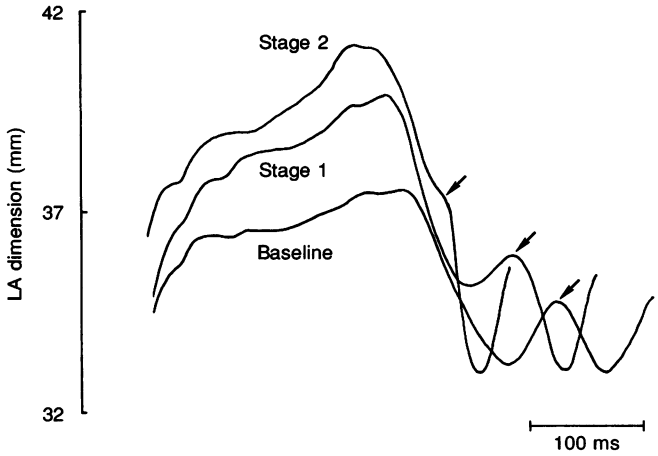

Figure 2
Superimposed tracings of left atrial (LA) diameter during a cardiac cycle at baseline and two levels of exercise from a representative animal.

Recent studies have demonstrated that downward motion of the mitral annulus is closely associated with the movement of blood from the pulmonary vein into the LA (Tsakiris, Gordon, Padiyar, Frechette & Labrosse, 1978; Keren, Sherez, Megidish, Levitt & Leniado, 1985; Smallhorn, Freedom & Olley, 1987; Keren, Sonnenblick & LeJemtel, 1988). To examine whether changes in mitral annular motion during exercise contributed to the changes we observed, a pair of ultrasonic dimension crystals (LTD-2, Transducer Products) were implanted on the LV apex and base in four animals.

Statistics

All data are presented as means ± one standard deviation. Differences between baseline and each stage of exercise were tested by repeated-measures analysis of variance. If a significant F value was obtained, Student's paired t test was used to identify where differences occurred. A value of $P < 0{\cdot}05$ was considered to indicate statistical significance.

RESULTS

Haemodynamics

Haemodynamic data are summarized in Table 1. The heart rate increased from 119 ± 14 beats min^{-1} at baseline to 168 ± 16 at stage 1, and 198 ± 13 at stage 2 ($P < 0{\cdot}005$ *vs.* baseline for both). Although the increase in mean aortic blood pressure was not significant at stage 1, it was at stage 2 ($P < 0{\cdot}05$). Cardiac output and stroke volume increased progressively during each stage of exercise. Although exercise caused no change in LV end-diastolic dimension, the decrease in end-systolic dimension became significant at stage 2 ($P < 0{\cdot}005$). The time constant of the LV pressure fall (T) decreased and dLVD/dt_{max} increased at each stage of exercise. These data indicate that exercise resulted in increases in LV pump function, the rate of LV relaxation and LV filling. The extent of shortening of the LV apex–base dimension increased progressively with each stage of exercise (3·3 ± 2·1 mm at baseline to 3·9 ± 2·1 mm at stage 1, and 4·8 ± 2·1 mm at stage 2; $P < 0{\cdot}01$ for stages 1 and 2 *vs.* baseline, $P < 0{\cdot}01$ for stage 2 *vs.* stage 1).

Typical tracings of LA dimension from a representative animal are shown in Fig. 2. Data are superimposed both at baseline and during exercise. The maximum LA dimension during systole for all animals studied increased at each level of exercise (40·7 ± 2·5 mm at baseline *vs.* 42·3 ± 3·1 mm at stage 1, $P < 0{\cdot}05$; *vs.* 43 ± 3·5 mm at stage 2, $P < 0{\cdot}05$; stage 1 *vs.* stage 2, $P < 0{\cdot}05$). The LA dimension at the onset of LA contraction increased significantly at stage 2 (39·1 ± 3·1 mm at baseline *vs.* 41·1 ± 2·6 mm at stage 2, $P < 0{\cdot}05$). Exercise caused no change in the minimum LA

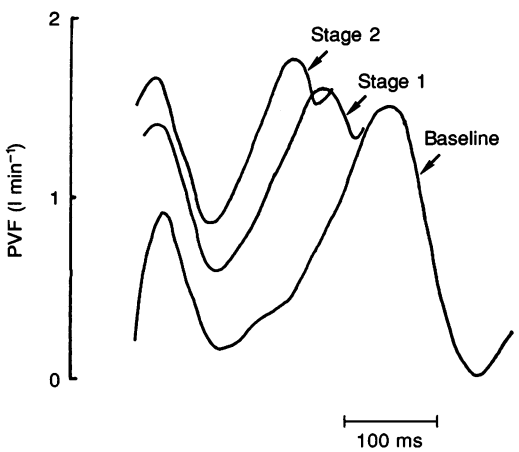

Figure 3
Superimposed tracing of pulmonary venous blood flow (PVF) at baseline and two stages of exercise in a representative animal.

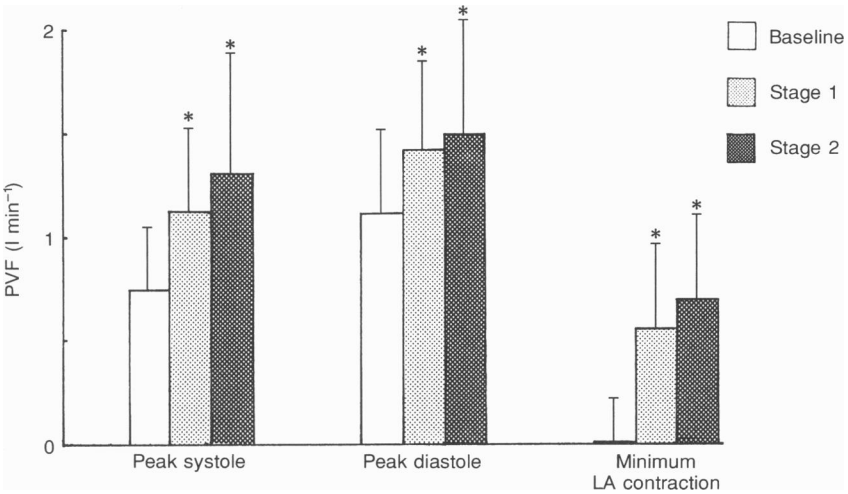

Figure 4
Changes in the peak pulmonary venous blood flow (PVF) during systole and during diastole, and the minimum flow during left atrial (LA) contraction. * *vs.* baseline, $P < 0.05$.

dimension during LA contraction. The LA dimension at the onset of LA contraction was linearly related to the maximum LA dimension during ventricular systole ($r = 0.61$, $P < 0.05$). These changes in LA dimension indicate that during exercise (1) more blood volume was reserved in the LA during systole, (2) LA preload at the onset of LA contraction increased and this change was associated with an increase in LA reservoir function, and (3) the extent of LA dimensional shortening increased.

Although the mean LA pressure, mean LA pressure during systole, LA pressure at the *y*-descent and peak a-wave pressure, were unchanged during exercise, the decrease in LA pressure at the *x*-descent became significant by stage 2 (4.9 ± 3.7 *vs.* 3.0 ± 4.4 mmHg, $P < 0.05$). Peak 'v-wave' pressure (the atrial pressure wave caused by LA filling during ventricular contraction) increased gradually during each stage of exercise (10.6 ± 4.5 mmHg at baseline to 12.8 ± 4.6 mmHg at stage 1, and 14.4 ± 4.2 mmHg at stage 2; $P < 0.05$ for stages 1 and 2 *vs.* baseline, $P < 0.05$ for stage 1 *vs.* stage 2). We calculated an effective (mean systolic) LA compliance index by dividing mean LA diameter during ventricular systole by mean LA pressure during that time. 'Effective' LA compliance is defined as LA compliance including pericardial and other influences. The effective LA compliance index increased during exercise compared to baseline (5.2 ± 0.4 mm mmHg^{-1} at baseline to 6.6 ± 0.6 mm mmHg^{-1} at stage 1, and 6.4 ± 0.6 mm mmHg^{-1} at stage 2; $P < 0.05$ for stages 1 and 2 *vs.* baseline). Taken together these findings suggest that (1) effective LA chamber compliance during ventricular systole increases, and (2) the driving pressure for PVF during systole tends to increase during exercise.

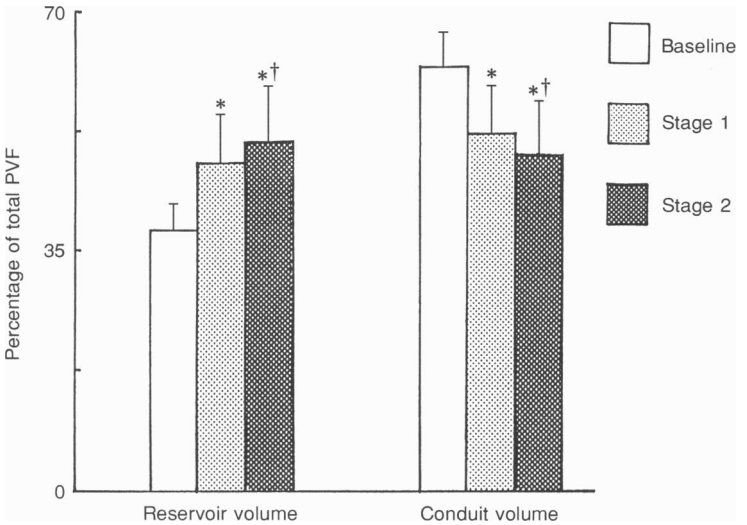

Figure 5
Changes in reservoir volume and conduit volume during exercise. * *vs.* baseline, $P < 0.05$; † *vs.* stage 1, $P < 0.05$.

Reservoir and conduit function

The typical pattern of PVF from a representative animal during exercise is shown in Fig. 3. Each tracing begins at end-diastole. Although exercise caused increases in blood flow during both systole and diastole, the increase was greater during systole than during diastole. The retrograde flow that is frequently present during LA contraction at rest was absent during exercise and instead blood flow during LA contraction increased progressively with each stage of exercise. The averaged data for all animals are shown in Figs 4–6. Both the peak systolic and diastolic blood flow increased during exercise ($P < 0.05$, Fig. 4). Although these parameters were higher at stage 2 than at stage 1, the difference did not reach statistical significance. As noted, the minimum flow during atrial contraction was almost zero at baseline (0.01 ± 0.22 l min^{-1}), but became very positive during exercise. Reservoir volume, as a percentage of the total volume of PVF, increased progressively during exercise (from $38 \pm 4\%$ at baseline to $48 \pm 7\%$ at stage 1, and $52 \pm 8\%$ at stage 2, Fig. 5) and conduit volume, as a percentage of the total volume of PVF, decreased during exercise (from $62 \pm 5\%$ at baseline to $52 \pm 7\%$ at stage 1, and $48 \pm 8\%$ at stage 2). This indicates that during exercise more blood was reserved in the LA during systole (increased reservoir function) and the percentage of the blood volume transported directly from the pulmonary vein through the LA into the LV during diastole decreased (decreased conduit function).

The mean systolic PVF increased progressively for all animals during each stage of exercise (0.52 ± 0.14 l min^{-1} at baseline to 0.85 ± 0.3 l min^{-1} at stage 1, and 1.0 ± 0.4 l min^{-1} at stage 2; $P < 0.01$ for stages 1 and 2 *vs.* baseline, $P < 0.05$ for stage 2 *vs.* stage 1). The mean diastolic PVF also increased during exercise (from 0.71 ± 0.26 l min^{-1} at baseline to 1.03 ± 0.44 l min^{-1} at stage 1, and 1.07 ± 0.4 l min^{-1} at stage 2; $P < 0.01$ for stages 1 and 2 *vs.* baseline). When expressed as a percentage increase over the corresponding baseline data (Fig. 6), the increase in the mean systolic blood flow was higher than was the increase in mean diastolic blood flow at stage 1 (62 ± 23 *vs.* $44 \pm 22\%$, $P < 0.05$), and stage 2 (93 ± 50 *vs.* $51 \pm 38\%$, $P < 0.05$). Thus, the increase in percentage reservoir volume and the decrease in percentage conduit volume was caused not only by a greater decrease in diastolic interval than systolic interval as heart rate increased during exercise, but also by a greater increase in the LA systolic filling rate than in the diastolic filling rate.

Booster function

The second half of the LV filling fraction increased from $33 \pm 10\%$ at baseline to $43 \pm 10\%$ at stage 1, and $52 \pm 11\%$ at stage 2 ($P < 0.005$). The relative change in early *vs.* late LV filling could have been caused by an increase in late filling, a decrease in early filling, or both. The peak shortening rate of LA diameter during atrial contraction increased from 59 ± 13 mm s^{-1} at baseline to 84 ± 24 mm s^{-1} at stage 1 ($P < 0.05$ *vs.* baseline), and 107 ± 26 mm s^{-1} at stage 2 ($P < 0.01$ *vs.* baseline, $P < 0.05$ *vs.* stage 1) during exercise. The peak lengthening rate of LA diameter during LA relaxation increased during exercise (79 ± 19 mm s^{-1} at baseline, 99 ± 27 mm s^{-1} at stage 1, and 117 ± 30 mm s^{-1} at stage 2; $P < 0.05$ for stages 1 and 2 *vs.* baseline).

DISCUSSION

In contrast to LA booster function, the non-contractile aspects of LA function have received little attention (Grant *et al.* 1964; Payne *et al.* 1971; Toma *et al.* 1989). The importance of LA compliance in regulating cardiac output was first demonstrated by Brighton and co-workers (Brighton, Wade, Pierce, Phillips & O'Bannon, 1973). In his study the addition of a flexible atrium to the inlet of an artificial heart substantially improved the cardiac output. Suga (1974), using an analog electronic model of the circulation, reported that the cardiac output increased from 2400 to 3240 ml min^{-1} and atrial pressure decreased from 3·0 to 2·2 mmHg when atrial compliance was

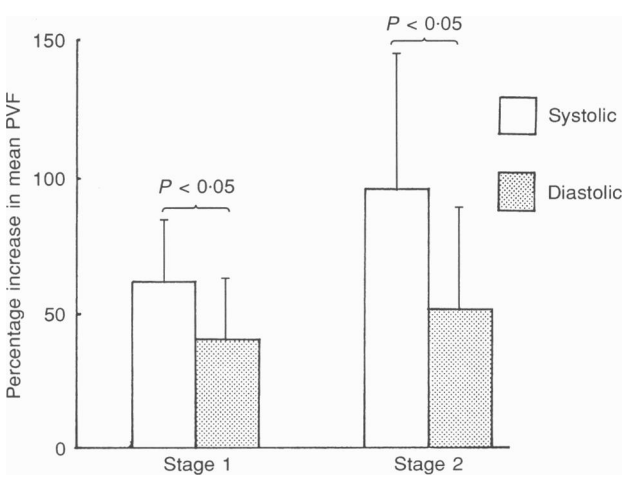

Figure 6
The percentage increase in mean systolic pulmonary venous blood flow (PVF) and diastolic flow during exercise.

increased from 1·0 to 20 ml $mmHg^{-1}$ with a constant resistance to venous return. These two studies clearly indicate that cardiac output could be markedly improved simply by increasing atrial compliance despite a constant ventricular contractility. Our study showed that LA dimension increased during exercise with no increase in LA pressure during ventricular systole. Although we could not measure the intrapericardial pressure surrounding the LA and thus do not know the exact change in transmural atrial pressure, our data demonstrate that the calculated effective mean LA chamber compliance increased during exercise. Exercise caused a decrease in LV volume during systole, and tended to decrease intrapericardial pressure. This change must have decreased pericardial restraint of the LA and may, in part, explain the increase in the calculated effective systolic LA chamber compliance we found during exercise. The exact role played by the pericardium in determining the effective atrial compliance is not presently known. This is a fundamentally important consideration that will require further study.

It is now quite clear that there are regional variations in intrapericardial pressure (Hoit, Bhargava, Dalton & Shabetai, 1989) euvolaemic animals operate on the 'flat' portion of the pericardial pressure–volume curve (Applegate, Santamore, Klopfenstein & Little, 1990) and easily move up to the steeper portion of the curve and to higher measured or calculated intrapericardial pressures in situations associated with increased total cardiac volumes (Applegate, Johnston, Vinten-Johansen, Klopfenstein & Little, 1992), and the pericardium is anisotropic being more difficult to stretch (less compliant) in the apex to base axis (Douglas, Lew, Ban-Hayashi, Shabetai, Waldman & LeWinter, 1986) in most evaluated animals. This combination of characteristics could contribute to an efficient coupling of LA and LV function (that may be modulated by adjustment in total cardiac volume). An increase in LV size during diastole would 'push' on the pericardium which (since it is stiffer in the longitudinal direction) would increase intrapericardial pressure surrounding the LA, decreasing 'effective' LA compliance and facilitating LA emptying. During ventricular systole, the LV decreases in size as blood is ejected and, by the same mechanism, reduces the intrapericardial pressure surrounding the LA, increasing 'effective' LA compliance to enhance LA filling. Thus, the pericardium would give the LV something to push (or not push) against to facilitate the emptying (or filling) of the LA and the movement of blood from the pulmonary veins to the LA and on to the LV. This mechanism is consistent with our data but cannot be truly tested during exercise because of the present lack of a method to correctly measure phasic regional intrapericardial pressure.

An increase in LA compliance during systole would have three advantages. First, it would allow LA pressure to stay low longer during systole, thus maintaining the gradient between the pulmonary vein and the LA and allowing a greater accumulation of blood in the LA before mitral valve opening. Second, this change would tend to maintain LA pressure higher than LV pressure for a longer time after mitral valve opening, enhancing early ventricular filling (Ishida *et al.* 1986). The increase in peak v-wave pressure observed in this study supports this concept. Finally, it also determines preload for LA contraction and therefore is an important determinant of the strength of LA contraction. Thus, atrial reservoir function, which is clearly dependent on atrial compliance, is a key determinant of cardiac systolic performance, because it can influence the volume of blood that flows from the LA to the LV during diastole. In this study using a conscious canine model with intact reflexes, we have found evidence of relative increases in both reservoir and booster functions during exercise, but not in conduit function. Increased reservoir function appeared to be related to increased preload for LV early filling as well as increased preload for LA contraction.

The observed changes in LV systolic and diastolic function, manifested by augmented LV ejection parameters and a decrease in the time constant of LV myocardial relaxation, are consistent with two recent studies using conscious dogs exposed to treadmill exercise (Miyazaki, Guth, Miura, Indolfi, Schulz & Ross, 1990; Cheng, Igarashi & Little, 1992). In our study the LV end- diastolic dimension did not change and the end-systolic dimension decreased during exercise. This is different from findings reported previously (Miyazaki *et al.* 1990; Cheng *et al.* 1992) in which the LV end-diastolic volume or segment lengths increased and those observed at end-systole did not change. One likely explanation for this discrepancy is the presence of pericardial restraint in our model. The pericardium was left wide open in previous models.

Mechanisms of increased reservoir function

Previous studies in anaesthetized animals have shown that an increase in heart rate to 180 beats min^{-1} caused a decrease in maximal atrial diameter during systole with progressively reduced atrial filling and depressed atrial emptying (Leistad, Christensen & Ilebekk, 1991). Thus, the changes we observed in atrial dimension during exercise were quite different from those found when heart rate alone was increased. During exercise the maximal atrial diameter increased, in association with augmentation of blood flow to the LA and increased LV filling.

It has been suggested that two mechanisms control LA filling dynamics. The first is forward transmission of pressure from the right ventricle through the pulmonary vasculature (Morkin *et al.* 1965; Guntheroth, Gould, Butler & Kinnen, 1974), and the second is a suction effect caused by the LA and LV throughout the cardiac cycle (Rajagopalan, Friend, Stallard & Lee, 1979*b*, *c*). Recent investigations have revealed little contribution of the

right side of the heart to LA inflow. Instead it appears to be mainly regulated by dynamic changes in LA pressure caused by contraction and relaxation of both the LA and LV (Keren *et al.* 1985; Smallhorn *et al.* 1987). Using Doppler echocardiography Keren *et al.* (1985) observed that the systolic component of PVF was greatly diminished and only the diastolic wave contributed to LA filling in patients without atrial contraction. They concluded that systolic inflow from the pulmonary vein to the LA while the mitral valve is closed is a reflection of the reduced pressure in the LA that results from relaxation of the LA. Inotropic stimulation with isoprenaline (isoproterenol) in dogs with an effective atrial contraction augmented the systolic component of PVF (Rajagopalan *et al.* 1979*c*). When atrial contraction is inhibited by stimulation of the left vagus nerve, the bulk of pulmonary venous blood flow occurs during ventricular diastole (Rajagopalan *et al.* 1979*c*). These data also support the idea that LA filling during systole is influenced by dynamic changes in LA pressure caused by contraction and relaxation of the LA. Enhanced contraction and relaxation of the LA would be expected to occur during exercise, and may result in a more rapid fall in LA pressure following atrial systole and an increase in flow from the pulmonary vein to the LA during early ventricular systole. We demonstrated that the peak lengthening rate of LA diameter (following LA contraction) increased during exercise along with an increase in the rate of LA dimensional shortening, suggesting that both the rate of atrial contraction and relaxation increased during exercise. Accelerated atrial relaxation during exercise plays an important role in enhancing reservoir function because it facilitates an increased movement of blood from the pulmonary vein to the LA.

Tsakiris *et al.* (1978) have demonstrated that during ventricular contraction, the mitral annulus moves towards the LV apex causing an increase in LA area. These changes in LA area were correlated with the magnitude of the displacement of the mitral annulus. Doppler echocardiography has clearly shown that in patients with dilated cardiomyopathy, PVF during systole (the J-wave) decreases and the diastolic wave (K-wave) becomes dominant. This has been associated with a markedly decreased movement of the mitral annulus towards the apex (Keren *et al.* 1988). In the absence of atrial contraction, some patients still show reduced but forward PVF during systole (Keren *et al.* 1985, 1988). These data suggest that downward movement of the mitral annulus by LV contraction also contributes to LA filling during systole. The increase in LV long-axis shortening and decrease in LA pressure at the time of x-descent which was observed during exercise in the present study support the concept that increased motion of the mitral annulus towards the apex plays an important role in increasing reservoir function during exercise by increasing the pulmonary vein to LA pressure gradient during systole. Thus, both LA relaxation and LV contraction must play a role in generating the systolic phase of the PVF during exercise.

Changes in conduit function

Morkin *et al.* (1965) demonstrated that contrast material passes from the pulmonary vein directly through the LA into the LV during ventricular diastole. This observation supports the hypothesis that, during ventricular filling, the atrium acts as an open conduit through which blood flows directly from the pulmonary vein though the mitral valve into the LV. Nishimura and co-workers (Nishimura, Abel, Halte & Tijik, 1990) reported that the peak diastolic velocity and deceleration time of blood in the pulmonary vein were similar to the peak velocity and deceleration time of the first wave of transmitral blood flow (E wave). Thus, it appears likely that LA conduit function is influenced by the same factors that determine early filling of the LV, such as LV relaxation, LA pressure, and viscoelastic properties of the myocardium. In this study an exercise-induced increase in early LV filling (taken from the peak lengthening rate of the LV diameter) was associated with an increase in the diastolic PVF rate. However, due to a simultaneous decrease in the time that was available for blood to pass from the pulmonary vein directly to the LV (the diastolic interval), relative conduit volume decreased during exercise.

Increased booster function during exercise

The atrial contribution to LV filling in humans, assessed by Doppler echocardiography, is relatively low at rest but increases from 10% at age 20 to as high as 46% at 80 years of age (Kuo, Quinones, Rokey, Sartori, Abinader & Zoghbi, 1987). Early studies have shown that when atrial fibrillation is converted to sinus rhythm, with little change in ventricular heart rate, there is still a measurable difference in cardiac output, especially during exercise (Hecht, Osher & Samuels, 1951) suggesting that atrial systole plays a more important role in maintaining cardiac output during exercise than at rest. Previous studies in humans have demonstrated that the percentage of second-half filling volume increases during supine bicycle exercise (Carroll, Hess, Hirzel & Krayenbuehl, 1983). Additional recent studies with Doppler recordings of transmitral blood flow velocity in normal subjects suggest that the contribution of atrial systole to overall transmitral blood flow progressively increases during mild exercise (Channer & Jones, 1989). Our animals had an increase in the relative amount of LV filling during the second half of diastole associated with an increase in the rate of shortening of LA diameter. We also found that the early filling rate of the LV increased during exercise. Thus, our data indicate that although exercise caused augmentation of both early and late filling, the increase in late filling was greater. An increased contribution of atrial systole to LV filling has also been suggested in the presence of a damaged or less compliant

LV caused by myocardial infarction (Rahimtoola *et al.* 1975), or myocardial hypertrophy (Hanrath, Mathey, Siegert & Bleifeld, 1980). In these conditions, LV diastolic abnormalities are characterized by prolonged myocardial relaxation or impaired early filling dynamics. Thus, augmented atrial booster function is considered to be an important mechanism compensating for impaired early diastolic filling, thus optimizing cardiac performance. The change in atrial booster function during exercise is uniquely different from these other settings, since during exercise an increased atrial contribution is associated with an increased rather than a decreased rate of LV relaxation and early filling of the LV. Furthermore, the retrograde PVF that was present at rest during atrial contraction was not seen during exercise despite increased LA contraction. In fact, the minimum level of PVF rose progressively with increasing levels of exertion even though atrial blood pressure at that time did not change significantly. This probably resulted from an increase in the forward inertia of pulmonary venous blood as the forward blood flow rate increased during exercise.

Mechanisms for increased atrial booster function

Linden & Mitchell (1960) have shown in anaesthetized open-chest dogs that when LV end-diastolic pressure was low, atrial systole caused greater changes in LV fibre length than when LV end-diastolic pressure was high. Doppler echocardiographic measurements have shown the ratio of passive to active transmitral blood flow velocity to be directly related to LV preload (Stoddard, Pearson, Kern, Ratcliff, Mrosek & Labovitz, 1989). Thus, the relative change in the atrial contribution depends on when atrial systole occurs on the LV diastolic pressure–volume curve. In this study, changes in LV preload cannot be responsible for the increased LA booster function during exercise because the LV end-diastolic volume did not change significantly during exercise. Previous studies have shown that the atria respond in the same way as the LV to stretch (Blinks, 1961; Payne *et al.* 1971) and to autonomic influences (Sarnoff, Brockman, Gilmore, Linden & Mitchell, 1960). Augmented LA reservoir function during exercise helped to maintain LA preload resulting in an increase in shortening through the Frank–Starling mechanism (Blinks, 1961). In other words, a marked increase in left atrial filling during ventricular systole tends to offset the decrease in LV preload which would have resulted from a shortened diastolic period as heart rate increased during exercise. Our data indicate that an increase in atrial booster function occurred and was due to combined effects of increased LA preload and (presumably) increased sympathetic stimulation.

Experimental preparation

In this study, we used an ultrasonic transit-time flowmeter to measure PVF (Drost, 1978). This technique has several advantages for the measurement of PVF when compared with other methods. First, it does not require physical contact with the vessel, and thus the critical effects on vessel shape and function caused by mechanical contact by the probe and of reactive fibrosis on vascular resistance are avoided. We selected the appropriate probe size at the time of surgery and made sure that there was no perivascular fibrosis at the time of postmortem examination. Second, the device measures volumetric blood flow independently of vessel size, vessel alignment and flow profile. Because the diameter of the pulmonary veins changes markedly during the cardiac and respiratory cycles in response to changes in transmural pressure (Rajagopalan, Bertram, Stallard & Lee, 1979*a*), measurement of blood velocity is not sufficient to determine changes in instantaneous volumetric blood flow. These characteristics and the zero stability of the transit-time flow measurement system make it the most appropriate method for measurement of PVF.

It has been demonstrated that the pericardium can modify the passive LV pressure–volume relationship (Shirato, Shabetai, Bhargara, Franklin & Ross, 1978) and has a considerable effect on the pattern of LV filling. Removal of the pericardium results in an enhancement of mid to late diastolic filling (Lavine, Campbell, Kloner & Gunther, 1988). Since the LA is a thin-walled structure, one may speculate that the pericardium has a greater influence on the LA than on the LV. We closed or approximated the pericardium in this study so that the changes in LA function observed would be similar to those in individuals with intact pericardia and intact reflexes. We found no differences between the responses of animals with sealed pericardia and animals with approximated pericardia suggesting that pericardial function had not been significantly altered.

In conclusion, dynamic exercise caused augmentation of LA reservoir and booster function. Increased LA reservoir function played an important role in increasing LV filling since it was associated with augmentation of early LV filling and also increased preload for LA contraction.

REFERENCES

Applegate, R. J., Johnston, W. E., Vinten-Johansen, J., Klopfenstein, H. S. & Little, W. C. (1992). The restraining effect of the intact pericardium during acute volume loading. *American Journal of Physiology* **262**, H1725–1733.

Applegate, R. J., Santamore, W. P., Klopfenstein, H. S. & Little, W. C. (1990). External pressure of the undisturbed left ventricle. *American Journal of Physiology* **258**, H1079–1086.

Benchimol, A., Ellis, J. G. & Dimond, E. G. (1965). Hemodynamic consequences of atrial and ventricular pacing in patients with normal and abnormal hearts. Effect of exercise at a fixed atrial and ventricular rate. *American Journal of Medicine* **39**, 911–922.

Blinks, J. R. (1961). Method for study of contraction of isolated heart muscle under various physical conditions. *Circulation Research* **9**, 342–348.

Brighton, J. A., Wade, Z. A., Pierce, W. S., Phillips, W. M. & O'Bannon, W. (1973). Effect of atrial volume on the performance of a sac-type artificial heart. *Transactions of the American Society for Artificial Internal Organs* **19**, 567–572.

Carroll, J. D., Hess, O. M., Hirzel, H. O. & Krayenbuehl, H. P. (1989). Dynamics of left ventricular filling at rest and during exercise. *Circulation* **68**, 59–67.

Channer, K. S. & Jones, J. V. (1989). The contribution of atrial systole to mitral diastolic blood flow increases during exercise in humans. *Journal of Physiology* **411**, 53–61.

Cheng, C. P., Freeman, G. L., Santamore, W. P., Constantinescu, M. S. & Little, W. C. (1990). Effect of loading conditions, contractile state, and heart rate on early diastolic left ventricular filling in conscious dogs. *Circulation Research* **66**, 814–823.

Cheng, C. P., Igarashi, Y. & Little, W. C. (1992). Mechanism of augmented rate of left ventricular filling during exercise. *Circulation Research* **70**, 9–19.

Douglas, M., Lew, W., Ban-Hayashi, E., Shabetai, R., Waldman, L. & LeWinter, M. M. (1986). *In vivo* mechanical behavior of canine pericardium. *American Journal of Physiology* **251**, H349–356.

Drost, C. J. (1978). Vessel diameter-independent volume flow measurement using ultrasound. In *Proceedings of San Diego Biomedical Symposium*, vol. 17, pp. 299–302. San Diego Biomedical Society, San Diego, CA, USA.

Grant, C., Bunnell, I. L. & Greene, D. G. (1964). The reservoir function of the left atrium during ventricular systole. An angiographic study of atrial stroke volume and work. *American Journal of Medicine* **37**, 36–43.

Guntheroth, W. G., Gould, R., Butler, J. & Kinnen, E. (1974). Pulsatile flow in pulmonary artery, capillary, and vein in the dog. *Cardiovascular Research* **8**, 330–337.

Hanrath, P., Mathey, D. G., Siegert, R. & Bleifeld, W. (1980). Left ventricular relaxation and filling pattern in different forms of left ventricular hypertrophy: An echocardiographic study. *American Journal of Cardiology* **45**, 15–23.

Hecht, H. H., Osher, W. J. & Samuels, A. J. (1951). Cardiovascular adjustments in patients with organic heart disease before and after conversion of atrial fibrillation to normal sinus rhythm. *Journal of Clinical Investigation* **30**, 647–648.

Hoit, B. D., Bhargava, V., Dalton, N. & Shabetai, R. (1989). Influence of the pericardium on dynamic right and left ventricular filling. *Journal of the American College of Cardiology* **13**, 207A.

Ishida, Y., Meisner, J. S., Tsujioka, K., Tallo, J. I., Yoran, C., Frater, R. W. M. & Yellin, E. L. (1986). Left ventricular filling dynamics: Influence of left ventricular relaxation and left atrial pressure. *Circulation* **74**, 187–196.

Keren, G., Sherez, J., Megidish, R., Levitt, B. & Laniado, S. (1985). Pulmonary venous flow pattern – Its relationship to cardiac dynamics: A pulsed Doppler echocardiographic study. *Circulation* **71**, 1105–1112.

Keren, G., Sonnenblick, E. H. & LeJemtel, T. H. (1988). Mitral annulus motion: Relation to pulmonary venous and transmitral flows in normal subjects and in patients with dilated cardiomyopathy. *Circulation* **78**, 621–629.

Kuo, L. C., Quinones, M. A., Rokey, R., Sartori, M., Abinader, E. G. & Zoghbi, W. A. (1987). Quantification of atrial contribution to left ventricular filling by pulsed Doppler echocardiography and the effect of age in normal and diseased hearts. *American Journal of Cardiology* **59**, 1174–1178.

Lavine, S. J., Campbell, C. A., Kloner, R. A. & Gunther, S. J. (1988). Diastolic filling in acute left ventricular dysfunction: Role of pericardium. *Journal of the American College of Cardiology* **12**, 1326–1333.

Leistad, E., Christensen, G. & Ilebekk, A. (1991). Right and left atrial diameters during incremental atrial pacing in pigs. *American Journal of Physiology* **260**, H973–978.

Linden, R. J. & Mitchell, J. H. (1960). Relation between left ventricular diastolic pressure and myocardial segment length and observations on the contribution of atrial systole. *Circulation Research* **8**, 1092–1099.

Miyazaki, S., Guth, B. D., Miura, T., Indolfi, C., Schulz, R. & Ross, J. Jr (1990). Changes of left ventricular diastolic function in exercising dogs without and with ischemia. *Circulation* **81**, 1058–1070.

Morkin, E., Collins, J. A., Goldman, H. S. & Fishman, A. P. (1965). Pattern of blood flow in the pulmonary veins of the dog. *Journal of Applied Physiology* **20**, 1118–1128.

Nagano, T., Arakawa, M., Tanaka, T., Yamaguchi, M., Takaya, T., Noda, T., Miwa, H., Kagawa, K. & Hirakawa, S. (1989). Diastolic compliance of the left atrium in man: A determinant of preload of the left ventricle. *Heart and Vessels* **5**, 25–32.

Nishikawa, Y., Roberts, J. P., Tan, P. & Klopfenstein, H. S. (1993). Increased left atrial reservoir function during exercise. *Circulation* **88**, I-213.

Nishimura, R. A., Abel, M. D., Halte, L. K. & Tijik, A. J. (1990). Relation of pulmonary vein to mitral flow velocities by transesophageal Doppler echocardiography: Effects of different loading conditions. *Circulation* **81**, 1488–1497.

Payne, R. M., Stone, H. L. & Engelken, E. J. (1971). Atrial function during volume loading. *Journal of Applied Physiology* **31**, 326–331.

Rahimtoola, S. H., Ehsani, A., Sinno, M. Z., Loeb, H. S., Rosen, K. M. & Gunnar, R. M. (1975). Left atrial transport function in myocardial infarction. Importance of its booster pump function. *American Journal of Medicine* **59**, 686–694.

Rajagopalan, B., Bertram, C. D., Stallard, T. & Lee, G. D. (1979*a*). Blood flow in the pulmonary veins: III. Simultaneous measurements of their dimensions, intravascular pressure, and flow. *Cardiovascular Research* **13**, 684–692.

Rajagopalan, B., Friend, J. A., Stallard, T. & Lee, G. D. (1979*b*). Blood flow in the pulmonary veins: I. Studies in the dog and man. *Cardiovascular Research* **13**, 667–676.

Rajagopalan, B., Friend, J. A., Stallard, T. & Lee, G. D. (1979*c*). Blood flow in pulmonary veins: II. The influence of events transmitted from the right and left sides of the heart. *Cardiovascular Research* **13**, 677–683.

Sarnoff, S. J., Brockman, S. K., Gilmore, J. P., Linden, R. J. & Mitchell, J. H. (1960). Regulation of ventricular contraction. Influence of cardiac sympathetic and vagal nerve stimulation on atrial and ventricular dynamics. *Circulation Research* **8**, 1108–1122.

Sasayama, S., Ross, J. Jr, Franklin, D., Bloor, M. M., Bishop, S. & Dilley, R. B. (1976). Adaptions of the left ventricle to chronic pressure overload. *Circulation Research* **38**, 172–178.

Shirato, K., Shabetai, R., Bhargara, V., Franklin D. & Ross, J. Jr (1978). Alteration of the left ventricular diastolic pressure–segment length relation produced by the pericardium. Effects of cardiac distention and afterload reduction in conscious dogs. *Circulation* **57**, 1191–1198.

Smallhorn, J. F., Freedom, R. M. & Olley, P. M. (1987). Pulsed Doppler echocardiographic assessment of extraparenchymal pulmonary vein flow. *Journal of the American College of Cardiology* **9**, 573–579.

Stoddard, M. F., Pearson, A. C., Kern, M. J., Ratcliff, J., Mrosek, D. G. & Labovitz, A. J. (1984). Influence of alteration in preload on the pattern of left ventricular diastolic filling as assessed by Doppler echocardiography in humans. *Circulation* **79**, 1226–1236.

Suga, H. (1974). Importance of atrial compliance in cardiac performance. *Circulation Research* **35**, 39–43.

TAN, P., VINTEN-JOHANSEN, J. & KLOPFENSTEIN, H. S. (1990). Computer acquisition and analysis of cardiovascular hemodynamic and cardiac performance data. *Journal of the American College of Cardiology* **15**, 269A.

TOMA, Y., MATSUDA, Y., MORITANI, K., RYOKE, T., KATAYAMA, K., MIURA, T., OGAWA, H., MATSUDA, M., MATSUZAKI, M. & KUSUKAWA, R. (1989). Left atrial conduit function for left ventricular filling dynamics in patients with myocardial infarction. *Catheterization and Cardiovascular Diagnosis* **18**, 85–89.

TSAKIRIS, A. G., GORDON, D. A., PADIYAR, R., FRECHETTE, D. & LABROSSE, C. (1978). The role of displacement of the mitral annulus in left atrial filling and emptying in the intact dog. *Canadian Journal of Physiology and Pharmacology* **56**, 447–457.

WEISS, J. L., FREDERICKSEN, J. W. & WEISFELDT, M. L. (1976). Hemodynamic determinants of the time-course of fall in canine left ventricular pressure. *Journal of Clinical Investigation* **58**, 751–760.

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