LEFT VENTRICULAR MECHANOENERGETICS DURING ASYNCHRONOUS LEFT ATRIAL-TO-AORTIC BYPASS

Effects of pumping rate on cardiac workload and myocardial oxygen consumption

The purpose of this study was to analyze left ventricular energetics during asynchronous, pulsatile left atrial to aortic bypass in the failing heart with the use of the pressure-volume relationship. In 12 anesthetized Holstein calves (body weight 94 ± 7 kg), $10 \mu\text{m}$ microspheres ($3.3 \times 10^7 \pm 1.1 \times 10^7/100$ gm left ventricular weight) were injected into the left main coronary artery to induce heart failure. Baseline left ventricular end-systolic elastance significantly decreased from 7.9 ± 0.7 to 5.5 ± 0.4 mm Hg/ml 100 gm left ventricular weight. Left ventricular pressure was measured with a micromanometer, and ultrasonic dimension transducers measured left ventricular orthogonal diameters. Ellipsoidal geometry was used to calculate simultaneous left ventricular volume. End-systolic elastance, pressure-volume area, external work, potential energy, and myocardial oxygen consumption were analyzed during steady-state contractions. After pre-pulsatile left atrial to aortic bypass measurements were taken, the measurements were repeated during asynchronous pulsatile left atrial to aortic bypass at the maximal pumping rate (69 ± 13 beats/min) termed 100%, and then 80%, 60%, and 40% of the maximal pumping rate in the full to empty mode. With increases in pumping rate, pressure-volume area and external work proportionally decreased, whereas potential energy remained unchanged except for 100% of maximal pumping rate. Pressure-volume area correlated linearly with myocardial oxygen consumption during asynchronous pulsatile left atrial to aortic bypass ($r = 0.971$). As a result, pumping rate correlated linearly with conservation of myocardial oxygen consumption ($r = 0.998$). In conclusion, decreased pressure-volume area accounts for the reduction in myocardial oxygen consumption during asynchronous pulsatile left atrial to aortic bypass. Conservation of myocardial oxygen consumption is mainly attributed to the reduction of external work. (J THORAC CARDIOVASC SURG 1995;110:793-9)

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Left ventricular (LV) bypass reduces LV pressure work and myocardial oxygen consumption (Vo_2),¹⁻³ while maintaining systemic blood flow in cases where the native heart has been unable to maintain the

peripheral circulation.^{1,4} Furthermore, conservation of Vo_2 and increase in oxygen supply during LV bypass results in reduction of myocardial infarct expansion in the coronary occlusion model.⁵⁻⁷ However, during nonpulsatile LV bypass, a nonlinear relationship exists between bypass flow and Vo_2 ,³ although the maximal reduction of LV Vo_2 would be achieved with complete LV decompression.^{1,3}

Asynchronous pulsatile left atrial-to-aortic bypass (PLAAB) is one of the commonly used clinical modalities. However, the same data for clinical PLAAB is limited. Furthermore, how the reduction of LV workload modulates Vo_2 has not been studied quantitatively. Linear relation has been obtained between Vo_2 and LV workload in terms of pressure-volume (P-V) area.⁸⁻¹⁰ If pumping rate correlated linearly with a reduction of LV work, a linear

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Fig. 1. Experimental preparation. AO, Aorta; Balloon Catheter, a catheter for coronary sinus blood flow with an occlusion balloon; Inlet, an inlet cannula of left ventricular assist device (LVAD); IVC, inferior vena cava; LA, left atrium; LVP, left ventricular pressure; O₂ Saturation Catheter, oxygen saturation catheter for coronary sinus blood; Outlet, an outlet cannula of LVAD; PA, pulmonary artery; SVC, superior vena cava.

relation would be obtained between pumping rate and VO_2 . The purpose of this study was to analyze how pumping rate affects LV VO_2 and LV workload in the failing heart during PLAAB.

Material and methods

Experimental preparation. A total of 12 Holstein calves weighing from 88 to 112 kg (average 94 ± 7 kg) were studied. While the calves were anesthetized with halothane, endotracheal intubation was performed and ventilation was maintained with a volume respirator with 100% oxygen. A median sternotomy was performed, and the left internal thoracic artery was cannulated for aortic pressure monitoring. A Swan-Ganz (Baxter Healthcare, Edwards Div., Santa Ana, Calif.) catheter was inserted for thermodilution cardiac output. The azygous and hemiazygous veins were ligated. Reversible occluders were placed around the superior and inferior venae cavae.

Pulse-transit ultrasonic dimension crystals (4 mm diameter) made of 5 MHz piezoelectric crystals (LTZ-2; Transducer Products, Goshen, Conn.) were placed at the endocardial surface across the anteroposterior minor axis, septal-free wall minor axis, and base-apex major axis of the LV as shown in Fig. 1.^{11, 12, 15} The septal transducer was placed into the septum just to the right of the left anterior descending coronary artery and positioned as

near as possible to the LV endocardial surface midway between the anterior and posterior transducers. A micromanometer-tipped catheter (Model SPC-350; Millar Instruments, Inc., Houston, Tex.) with a pressure transducer unit (Model TCB-500; Millar Instruments, Inc.) was calibrated and balanced at 37° C with a mercury manometer and inserted into the LV through the LV free wall. The micromanometer was rechecked *in vivo* by correlation with the LV end-diastolic pressure signal obtained simultaneously through the fluid-filled polyethylene catheter connected to a pressure transducer (Model 041-500-503; Cobe, Lakewood, Colo.).

After anticoagulation with intravenous heparin (300 U/kg), a 14 mm assist pump outflow cannula was sutured to the ascending aorta. The 51F cannula for assist pump inflow was inserted through a pursestring into the left atrial appendage. The cannulas were connected to the inlet and outlet ports, respectively, of a Pierce-Donachy pneumatic pump to establish PLAAB.

To prevent dysrhythmia during the preparation, digoxin (0.25 mg, intravenously) and lidocaine (2.5 mg/min, intravenously) were administered. If needed, a constant infusion of epinephrine (0.01 to 0.04 $\mu\text{g/kg/min}$, intravenously), phenylephrine (0.3 to 1.0 $\mu\text{g/kg/min}$, intravenously), isoproterenol (0.002 to 0.01 $\mu\text{g/kg/min}$, intravenously) or a combination was used to prevent pulmonary hypertension and systemic hypotension during the experimental preparation.¹⁶ In all cases, the catecholamines were successfully weaned before data collection. To maintain systemic pressure and ventricular filling, adjustments of intravascular blood volume were made by infusion of whole blood. The hematocrit level was maintained at $35.7\% \pm 2.1\%$ during data collection.

All animals involved in this study received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Research and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985).

Experimental protocol. Pressure and volume data were taken by changing preload condition by gradually occluding superior and inferior venae cavae. Afterload condition was then altered by gradually occluding the aortic root with a vascular clamp. All data during caval and aortic occlusion was analyzed to determine the baseline end-systolic pressure-volume relationship (ESPVR) and LV unloaded volume. After control measurements, to induce heart failure, a 20-gauge Teflon catheter was passed proximally into the left main coronary artery through the left anterior descending coronary artery. An average of $3.3 \times 10^7 \pm 1.1 \times 10^7$ microspheres (10 μm , NEM-001; New England Nuclear, Boston, Mass.) per 100 gm LV was injected. After all tracings reached steady-state, pre-PLAAB measurements were performed.

Asynchronous PLAAB was established at a maximal pumping rate termed 100%, as limited by the pump filling from the left atrial cannula. We used a negative pressure (50 to 55 mm Hg negative pressure) to maximize the pump filling. Pumping rate was then decreased to 80%, 60%, and 40% of the maximal pumping rate. All measurements were repeated during steady-state conditions in

each setting of pumping rate. After cessation of PLAAB, second measurements without PLAAB were performed. Because no statistical difference was found between the first and second measurements, we used the first measurements as pre-PLAAB heart failure run.

At the conclusion of the experimental protocol, the animals were killed, and the hearts were excised to verify the proper positioning of the crystals and transducers.

Data analysis. All data were sampled simultaneously at 150 Hz and stored on a floppy disk by means of an on-line data acquisition system. Data were analyzed with interactive computer software developed in our laboratory.

Ultrasonic signals were continuously monitored with an ultrasonic dimension system (System 6 chassis with four sonomicrometer modules; Triton Technology, San Diego, Calif.) with the minimal resolution of 1 mm LV volume (LVV) calculated from the orthogonal endocardial diameters with the use of a modified ellipsoidal shell model^{11, 12, 15}.

$$LVV = \pi/6 \cdot D_L \cdot D_{AP} \cdot D_{SL}$$

where D_L , D_{AP} , and D_{SL} are base-apex major axis, anteroposterior minor axis, and septal-free wall minor axis orthogonal diameters of the LV, respectively.

LV mechanics. The ESPVR has been recognized as a load-independent index of contractile state.^{8, 13, 14} The contractile state of the LV was assessed by the ventricular end-systolic elastance, that is, the slope of the ESPVR. The LV unloaded volume¹⁷ is the volume intercept of the ESPVR. Practically, the slope of the ESPVR of each contraction was defined as the maximal slope relative to unloaded volume and normalized for 100 gm/LV weight.

Unloaded volume was determined by linear regression of end-systolic pressure and volume data at end-systole during pre-PLAAB measurement. Repetitive linear regressions were used to determine unloaded volume. Provisional end-systole was set at the timing of minimal LV compliance, LV volume/LV pressure. Then the first linear estimation of unloaded volume was used to determine end-systolic data points defined by the maximal pressure/(volume - unloaded volume) ratio in each cardiac cycle.¹⁸ Linear regression was repeated to determine a new estimate of unloaded volume that was then used to determine end-systole for a subsequent linear regression. We assumed the same unloaded volume during PLAAB as in pre-PLAAB conditions.

Fig. 2 shows the schematic diagram of PV area and VO_2 /P-V area relationship. P-V area is the area bounded by the end-systolic and end-diastolic P-V relations and the systolic segment of the P-V trajectory.^{8, 14, 16} P-V area has been recognized as a measure of total mechanical energy because P-V area correlates linearly with VO_2 in a stable contractile state regardless of changes in loading conditions.^{8-10, 16} We calculated P-V area of the beating LV by summing all small triangular areas swept by the lines connecting unloaded volume and instantaneous P-V data points during systole.¹¹ The crescent area between the actual end-diastolic P-V curve and the straight line connecting unloaded volume and the end-diastolic P-V point was approximated with a third power function.¹¹ This area was added to the sum of the small triangular areas to complete P-V area. P-V area consists of external work

Fig. 2. A, Schematic diagram of P-V relationship; B, schematic diagram of VO_2 /P-V area (PVA) relationship. Pressure, left ventricular pressure; EDPVR, end-diastolic P-V relationship; EW, external work; PE, potential energy; Volume, left ventricular volume; V_0 , X axis intercept of the end-systolic P-V relationship; VO_2 , myocardial oxygen consumption.

within the P-V loop and potential energy on the origin side of the loop. Potential energy is generated during contraction and has been assumed to dissipate as heat during relaxation. End-diastole was determined from the electrocardiogram. All the parameters were calculated in every cardiac cycle for 12 seconds and averaged data were subjected to statistical analysis. With the advantages of P-V area, the relation between LV work load and VO_2 during asynchronous PLAAB can be quantitatively analyzed.

Myocardial oxygen consumption. A 22F silastic balloon catheter (Argyle Co., St. Louis, Mo.) was inserted into the coronary sinus through a purse-string suture of the right atrium. The coronary sinus was totally occluded at the orifice by inflating a balloon to drain all sinus blood flow. An Optometric oxygen saturation catheter (Hospex Fiberoptics, Chestnut Hill, Mass.) was also inserted into the coronary sinus to measure coronary sinus oxygen saturation. VO_2 was calculated from the following formulations:

$$1) \text{ Arterial } O_2 \text{ content (Vol\%)} = \text{Arterial } O_2 \text{ saturation} \times \text{Hct}/3 \times K_1 + \text{PaO}_2 \times K_2$$

where K_1 is the binding coefficient = 1.39 ml O_2 /1 gm hemoglobin; K_2 is the solubility coefficient = 0.003 ml O_2 ; PaO_2 is arterial oxygen tension; and Hct is hematocrit value.

$$2) \text{ Venous } O_2 \text{ content (Vol\%)} = \text{Venous } O_2 \text{ saturation} \times \text{Hct}/3 \times K_1 + \text{PVO}_2 \times K_2$$

$$3) \text{ } VO_2 = \text{Arterial-venous } O_2 \text{ difference (Vol\%)} \times \text{coronary sinus flow (ml/min)}.$$

At the conclusion of each experiment, the heart was excised and all tissue was removed from the LV for weighing. VO_2 was normalized for 100 gm of LV wet weight for statistical analysis.

Statistics. Comparisons of variables among the groups were tested with two-way analysis of variance. When analysis of variance showed statistical significance by F test, mean values were compared by the least significance

Table I. Hemodynamic parameters during asynchronous left atrial to aortic bypass

	Control	Heart failure	PLAAB 100%	PLAAB 80%	PLAAB 60%	PLAAB 40%
Pump rate	NA	NA	69 ± 3	56 ± 2	42 ± 2	28 ± 1
HR (beats/min)	99 ± 13	97 ± 1	97 ± 1	99 ± 1	97 ± 1	97 ± 4
E_{max} (mm Hg/ml)	7.3 ± 0.2	5.5 ± 0.1*	5.0 ± 0.1*	4.9 ± 0.1*	4.7 ± 0.1*	4.6 ± 0.1*
EDV (ml)	110 ± 4	127 ± 3*	103 ± 3†	110 ± 4†	119 ± 3	123 ± 3*
ESV (ml)	86 ± 3	102 ± 3*	92 ± 3†	98 ± 3†*	105 ± 3*	106 ± 3*
EDP (mm Hg)	13.4 ± 0.6	14.4 ± 0.4*	7.3 ± 0.3†*	9.0 ± 0.3*	11.1 ± 0.3*	11.9 ± 0.3*
ESP (mm Hg)	64 ± 2	68 ± 2	51 ± 3†	55 ± 2	63 ± 2	64 ± 2
CVP (mm Hg)	6.9 ± 0.7	7.5 ± 0.8*	8.0 ± 0.6*	7.6 ± 0.7*	7.6 ± 0.7*	7.7 ± 0.7*
mAoP (mm Hg)	54 ± 4	55 ± 6	63 ± 6*	59 ± 6	59 ± 6	57 ± 6
CO (L/min)	6.7 ± 0.4	5.8 ± 0.5*	6.4 ± 0.5†	6.1 ± 0.5	5.9 ± 0.6*	5.9 ± 0.5*

Values are expressed as mean ± standard error of the mean. NA, Not available; E_{max} , slope of ESPVR; EDV, end-diastolic volume; ESV, end-systolic volume; EDP, end-diastolic pressure; ESP, end-systolic pressure; CVP, central venous pressure; HR, heart rate; mAoP, mean aortic pressure; CO, cardiac output.

* $p < 0.05$ compared with control.

† $p < 0.05$ compared with heart failure.

method. Probability values smaller than 0.05 were considered statistically significant. Data are presented as mean ± standard deviation unless otherwise indicated.

Results

Hemodynamic parameters in the control and heart failure runs and during each pumping rate in failing hearts are shown in Table I. Microsphere injection induced heart failure in which the slope of the ESPVR significantly decreased by $17\% \pm 31\%$ from the control run. As we administered whole blood to maintain systemic arterial pressure, end-systolic pressure did not significantly change and both end-systolic volume and end-diastolic volume significantly increased by $19\% \pm 16\%$ and $24\% \pm 19\%$, respectively. Despite whole blood transfusion, cardiac output significantly decreased by $22\% \pm 35\%$. The heart rate was unchanged between the control and heart failure runs. In 100% of rate, PLAAB significantly increased the cardiac output by $11\% \pm 16\%$. PLAAB significantly reduced end-diastolic pressure (by $32\% \pm 19\%$ and $42\% \pm 19\%$) and volume (by $15\% \pm 11\%$ and $20\% \pm 12\%$) during 80% and 100% of rate, respectively, compared with pre-PLAAB heart failure. End-systolic pressure and volume did not significantly differ except for 100% of rate. Heart rate, central venous pressure, and mean aortic pressure did not change between each pumping rate.

Fig. 3 shows mean P-V area, external work, and potential energy in all 12 experiments. PLAAB significantly decreased P-V area (pre-PLAAB, 870 ± 448 ; 40%, 705 ± 402 ; 60%, 648 ± 396 ; 80%, 497 ± 392 ; 100%, 430 ± 428 mm Hg/ml/100 gm LV) and external work (pre-PLAAB, 483 ± 287 ; 40%, $295 \pm$

202; 60%, 241 ± 180 ; 80%, 151 ± 144 ; 100%, 126 ± 152 mm Hg/ml/100 gm LV) with increases in pumping rate. However, potential energy did not significantly change except for 100% of rate. Therefore, the decreases in P-V area are mainly attributable to decreases in external work.

Fig. 4 shows a mean VO_2 /P-V area relationship derived from different settings of pumping rates (40% to 100%). Linear VO_2 /P-V area relationship ($r = 0.971$) indicated that reduction of P-V area accounts for the reduction of VO_2 during PLAAB. Pumping rate linearly correlated with VO_2 as in Fig. 5 ($r = 0.998$).

Discussion

The maximal conservation of LV VO_2 is known to be accomplished during the maximal ventricular unloading.³ However, it is not clear how the pumping rate of asynchronous PLAAB affects the relation between LV workload and VO_2 . In this study, we quantitatively analyzed the relationship between VO_2 and LV workload in terms of P-V area during asynchronous PLAAB. P-V area linearly correlated with VO_2 even during asynchronous PLAAB and decreases in P-V area reasonably accounted for the reduction of VO_2 . As P-V area inversely correlated with pumping rate, asynchronous PLAAB proportionally decreased VO_2 with increases in pumping rate. Furthermore, quantitative analysis of the effects of asynchronous PLAAB on P-V area clarified a limited decrease in potential energy during asynchronous PLAAB, which suggested a limited unloading of the LV.

A nonlinear relationship between VO_2 and LV unloading has been reported during nonpulsatile

Fig. 3. Comparison of left ventricular mechanics during pulsatile left atrial to aortic bypass. Values are expressed as means $\pm$ standard error of the mean. *PVA*, P-V area; *EW*, external work; *PE*, potential energy.

LV bypass.³ Major differences exist between non-pulsatile LV bypass with the use of a roller pump with a reservoir and asynchronous PLAAB. Nonpulsatile LV bypass with a reservoir totally decompresses the LV because the system enables continuous unloading of the LV. Conversely, PLAAB requires some period to empty the pump itself. Therefore, PLAAB only intermittently decompresses the LV, which would allow the LV to fill to some extent. As a result, the magnitude of LV unloading is determined by competing blood volume (preload) between the PLAAB and the native LV. Once the LV is filled with blood, PLAAB does not decompress the LV until the LV itself ejects the blood volume because PLAAB cannot directly drain blood through the mitral valve. In addition, pulsatile pressure generated by asynchronous PLAAB increases aortic pressure as afterload, which interferes with the native LV ejection. As a result, the native heart completes preload or afterload with asynchronous PLAAB according to the timing between pumping and native heart rates, which would account for the inability of asynchronous PLAAB to totally unload the LV as shown by limited decrease in potential energy. Therefore, some disadvantages would be expected in unloading LV during asynchronous PLAAB compared with complete unloading seen with nonpulsatile systems under the same circumstances. Further study is needed to evaluate the difference between the nonpulsatile LV bypass and PLAAB.

Fig. 4. Vo_2 /P-V area (*PVA*) relationship during pulsatile left atrial to aortic bypass. Dashed line represents 99% confidence limit line. Values are expressed as means $\pm$ standard error of the mean. $r = 0.971$; $Vo_2 = 2.14 \times 10^{-5} \times PVA + 0.0215$.

Fig. 5. The relationship between pumping rate and myocardial oxygen consumption. Dashed line represents 99% confidence limit line. Values are expressed as means $\pm$ standard error of the mean. $r = 0.998$; $Y = -9.61 \times 10^{-5} \times X + 0.0414$.

Because a linear correlation exists between pumping rate and P-V area, the ratio of Vo_2 conservation at a given pumping rate could be estimated as a relative value to that of the maximal pumping rate. When fluid replacement is made at a fixed pumping rate during asynchronous PLAAB, left atrial pressure (the native LV preload) significantly increases. Change in LV preload affects LV work load (P-V area) under a given pumping rate. Then, changes in the native LV preload would result in the alteration of the maximal pumping rate. The ratio of Vo_2 conservation at a given pumping rate would be variable depending on the preloading condition. The determination of the maximal pumping rate in

a given situation is important in determining Vo_2 conservation rate.

We measured the LV volume with an ellipsoidal geometry of the LV. This geometry might change in acute LV failure. Furthermore, the LV decompression with PLAAB could exaggerate the deformation of the LV geometry. However, we induced global damage of the LV by injecting microsphere in the left main coronary artery. Therefore, we assumed the LV damage was homogenous and therefore the deformation was minimal. During PLAAB, a large septal shift was possible to make the LV deformation. However, because we used the atrial cannula instead of a ventricular cannula, the LV was not totally decompressed even during maximal PLAAB. Our preliminary study showed the right ventricular pressure was mostly higher than the LV pressure. Thus we assume the septal shift would not affect the LV geometry in our experiment.

Because we determined the slope of ESPVR as the maximal slope relative to unloaded volume in each contraction during PLAAB, accurate unloaded volume was important to determine the slope of ESPVR correctly in each experiment. Unloaded volume was determined as a X axis intercept of the linear regression of the end-systolic P-V data in the pre-PLAAB condition. Unloaded volume value determined from a narrow range of data results in a large error in the estimate. Then, to achieve a wide range of pressure and volume data, both the transitional parts of 8 to 10 seconds' data during aortic and caval occlusions were subjected to the linear regression. Afterload condition ranged from 36 ± 7 mm Hg to 123 ± 26 mm Hg. Unloaded volume calculated in this manner reasonably estimates unloaded volume during PLAAB.¹⁶

Heart failure was induced by small-sized microsphere injection into the main left coronary artery. Further administration of intracoronary microsphere resulted in animal death in the middle of the experiment. The depression in hemodynamic parameters observed was comparatively small in our experiment. However, the heart failure model produced by this size of microsphere has outstanding features. Absence of myocardial necrosis in the histologic examination strongly suggests almost complete recovery from acute ischemic damage in the chronic phase.¹⁹ Attenuation of myocardial contractile and metabolic dysfunction with recombinant human superoxide dismutase^{20,21} indicates that the heart failure model we used is more likely to be related to chemical reaction than to the other

ischemic process obtained by coronary ligation. Although the difference was small, our model would be able to simulate myocardial stunning. Because this study simulated a global damage of LV, the effects of pumping rate on LV mechanics and Vo_2 might be different from results in the settings of local damage as a result of myocardial infarction or LV aneurysm. Thus, further study is needed to characterize true effects of asynchronous PLAAB in clinical settings.

In conclusion, there is a linear relation between pumping rate and conservation of Vo_2 during asynchronous PLAAB. Pumping rate-dependent decrease in P-V area during asynchronous PLAAB that accounts for the reduction of Vo_2 is mainly attributed to reduction of external work. Unchanged potential energy suggests a limited unloading of the ventricle during asynchronous PLAAB.

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