VENTRICULOARTERIAL COUPLING WITH INTRA-AORTIC BALLOON PUMP IN ACUTE ISCHEMIC HEART FAILURE

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Purpose: **We analyzed the mechanism of effects of intra-aortic balloon pumping using the pressure-volume relationship and ventriculoarterial coupling in the normal and failing hearts.** ***Materials:*** **In 12 anesthetized Holstein calves (weight, 94 ± 8 kg), the ventricular end-systolic and arterial elastances, pressure-volume area, and external work were analyzed during steady-state contractions with traditional hemodynamic parameters with intra-aortic balloon pumping–off and –on (1:1 synchronous ratio). An acute ischemic heart failure was induced by injecting 10 μm microspheres ($4.2 \pm 1.8 \times 10^7$ · 100g left ventricular weight^{-1}) into the left main coronary artery; all measurements were repeated.** ***Results:*** **Intra-aortic balloon pumping did not change hemodynamic parameters in the control. However, during heart failure, intra-aortic balloon pumping decreased the arterial elastance from 3.6 ± 1.3 mm Hg to 2.9 ± 1.2 mm Hg · mL^{-1} while not affecting the ventricular end-systolic elastance, this resulted in an improvement of the ventriculoarterial coupling ratio from 3.1 ± 0.8 to 2.3 ± 0.8. Intra-aortic balloon pumping decreased not only end-systolic pressure (from 69 ± 16 mm Hg to 64 ± 19 mm Hg) but end-diastolic volume and pressure (from 139 ± 38 mL to 137 ± 37 mL and from 13.9 mm Hg to 12.8 mm Hg, respectively) with the leftward shift of the pressure-volume loop. Pressure-volume area decreased (from 914 ± 284 mm Hg to 849 ± 278 mm Hg · mL) although stroke volume increased (from 21 ± 6 mL to 24 ± 6 mL).** ***Conclusion:*** **Reduction of the arterial elastance with intra-aortic balloon pumping improved the ventriculoarterial coupling ratio and increased stroke volume. Leftward shift of the pressure-volume loop resulted in the reduction of pressure-volume area, which suggests the conservation of the myocardial oxygen consumption. (J Thorac Cardiovasc Surg 1999;117:164-71)**

Intra-aortic balloon pumping (IABP) is a common method of circulatory support for acute failing hearts. The major effect of IABP is afterload reduction and a diastolic augmentation. The former indicates a low impedance shunt for the aortic blood during cardiac systole, which provides the mechanical unloading of the left ventricle (LV) by reducing the LV ejection pressure.[1,2] The latter elevates the perfusion pressure of the coronary artery to increase coronary blood flow,[3] and the reduction of cardiac work load is expected to reduce the need for oxygen.[4,5] Patients whose condition requires IABP after the coronary arterial bypass grafting may immediately benefit from increased coronary perfusion and reversal of acute ischemia. On the other hand, the unloading effect of IABP would be more important in patients after the valve operation. However, the data for IABP on the LV work load are limited, especially in the failing heart. The mechanism for the unloading effect with IABP is not completely understood. The purpose of this study was to evaluate the effect of IABP on LV work load by assessing changes in pressure-volume relationship and ventriculoarterial coupling.

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Materials and methods

Experimental preparation. A total of 12 Holstein calves weighing from 86 to 104 kg (average, 94 ± 8 kg) was studied. With the calf under halothane anesthesia, an endotracheal tube was inserted; the ventilation was maintained by a volume respirator with 100% oxygen. A median sternotomy was performed, and the left internal thoracic artery was cannulated for the aortic pressure monitoring. The azygos and hemiazigos veins were ligated. Reversible occluders were placed around the superior and inferior venae cavae.

As shown in Fig 1, 3 pairs of pulse-transit ultrasonic dimension crystals (4-mm diameter) made of 5 MHz piezoelectric crystals (LTZ-2; Transducer Products, Goshern, Conn) were placed at the endocardial surface (the anteroposterior minor axis, septal-free wall minor axis, and base-apex major axis of the LV).[6-8] Ultrasonic signals were continuously monitored with an ultrasonic dimension system (System 6 chassis with 4 sonomicrometer modules; Triton Technology, San Diego, Calif) with the minimal resolution of 1 mm. LV volume was calculated from the orthogonal endocardial diameters with a modified ellipsoidal shell model.[6-8]

$$\text{LV volume} = \pi/6 \times D_L \times D_{AP} \times D_{SL}$$

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.

After anticoagulation with intravenous heparin (300 units/kg), a micromanometer-tipped catheter (model SPC-350; Millar Instruments, Inc, Houston, Texas) with a pressure transducer unit (model TCB-500; Millar Instruments, Inc) was inserted into the LV through the LV free wall. The micromanometer was rechecked in vivo by correlation with the LV end-diastolic pressure signal simultaneously obtained through the fluid-filled polyethylene catheter connected to a pressure transducer (model 041-500-503; Cobe, Lakewood, Colo). An IABP (Kontron model 10; Arrow International, Reading, Pa) was inserted from the left femoral artery to the descending aorta. The position of the balloon pump was assured by pulsation.

To prevent arrhythmia during the preparation, digoxin (0.25 mg, intravenously) and lidocaine (2.5 mg/min, intravenously) were administered. To maintain systemic pressure and ventricular filling, adjustments of intravascular blood volume were made by infusion of whole blood. Hematocrit was maintained at 35.2% ± 2.7% during data collection. If needed to prevent systemic hypotension or pulmonary hypertension during the experimental preparation, a constant infusion of epinephrine (0.01 to 0.04 μg/kg per minute, intravenously), phenylephrine (0.3 to 1.0 μg/kg per minute, intravenously) and/or isoproterenol (0.002 to 0.01 μg/kg per minute, intravenously) were used.[7,8] In all cases, these drugs were successfully weaned before 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).

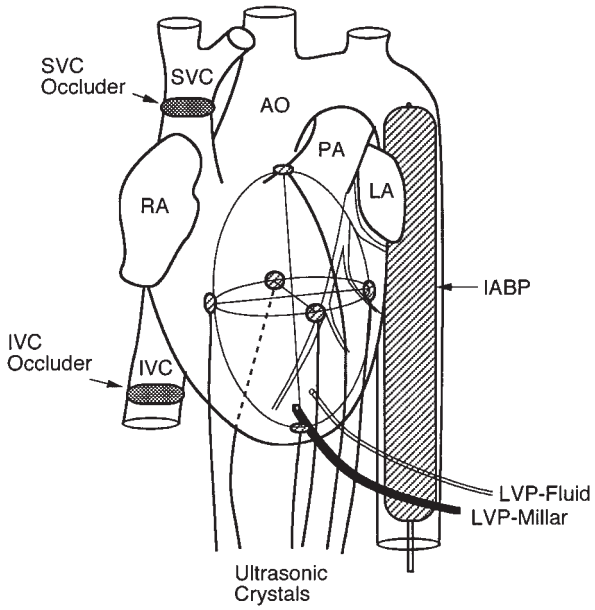

Fig 1. Experimental preparation. *SVC*, Superior venae cavae; *AO*, aorta; *PA*, pulmonary artery; *RA*, right atrium; *LA*, left atrium; *IVC*, inferior venae cavae; *LVP-Fluid*, a catheter for fluid-filled LV pressure; *LVP-Millar*, a manometer-tipped catheter for LV pressure.

Experimental protocol. When hemodynamic steady-state was achieved after the calves were weaned from catecholamines, caval and aortic occlusions were applied, and LV unloaded volume and V_0 were determined. Then end-systolic and end-diastolic volume and pressure, central venous pressure, mean aortic pressure, and the pressure-volume relationship (which includes end-systolic elastance, pressure-volume area, and external work [EW]) were assessed during steady-state beats. IABP was started with 1:1 synchronous ratio; all measurements were repeated as a control.

After baseline 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.[7-9] An average of $4.2 \pm 1.8 \times 10^7$ per 100 g LV-weight microspheres (10 μm, NEM-001; New England Nuclear, Boston, Mass) was injected. After all tracings reached steady-state, heart failure measurements were performed. At the conclusion of the experimental protocol, the animal was killed, and the heart was 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 via an on-line data acquisition system. Data were analyzed with interactive computer software that was developed in our laboratory.

LV mechanics. The contractile state of the LV was assessed by the ventricular end-systolic elastance, E_{max},

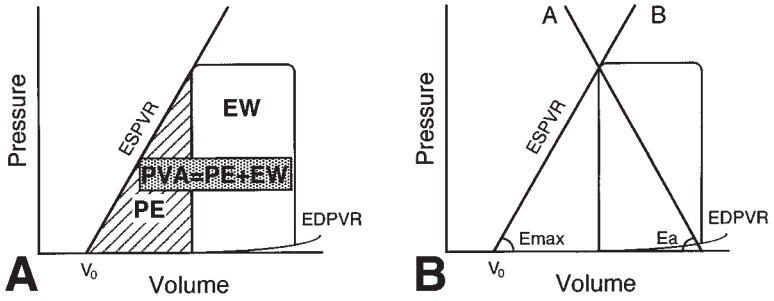

Fig 2. A, Schematic diagram of the pressure-volume relationship. *EDPVR*, End-diastolic pressure-volume relationship; *PVA*, pressure-volume area; *PE*, potential energy. **B**, Schematic diagram of the end-systolic ventricular and arterial elastance. The slope of the arterial end-systolic pressure-volume relationship (*ESPVR*; *line A*) is E_a with the volume intercept of end-diastolic volume. *Line B* represents the ventricular ESPVR, with the volume intercept of V_0.

which has been recognized as a load-independent index of contractile status (Fig 2).[10-12] Practically, E_{max} of each contraction was defined as the maximal slope relative to the LV unloaded volume, V_0, which is the volume intercept of the end-systolic pressure-volume relationship, and normalized for 100 g LV weight. V_0 was determined by the repetitive linear regression of end-systolic pressure and volume data at end systole during baseline measurement.

Pressure-volume area is the area bounded by the end-systolic and end-diastolic pressure-volume relationships and the systolic segment of the pressure-volume trajectory.[10,12,13] Because pressure-volume area linearly correlates with myocardial oxygen consumption in a stable contractile state regardless of changes in loading conditions, pressure-volume area has been recognized as a measure of total mechanical energy.[10,13-15] Pressure-volume area consists of EW within the pressure-volume loop and potential energy, a triangular area next to EW. The ratio of EW to pressure-volume area was calculated as an index of cardiac performance.[12,16] End-diastole was determined from the R wave of the electrocardiogram. All the parameters were calculated in every cardiac cycle for 12 seconds, and averaged data were subjected to statistical analysis.

Ventriculoarterial coupling. Effective arterial elastance, E_a, is defined as the ratio of end-systolic pressure to stroke volume.[17-19] Therefore the slope of the arterial end-systolic pressure-volume relationship is E_a with the volume axis intercept of end-diastolic volume although the ventricular end-systolic pressure-volume relationship has a slope of E_{max} with the volume axis intercept of V_0. Because E_a is related to the Windkessel parameters of the arterial system, E_a provides a quick and practical measure of the arterial properties.[19] Although E_a does not represent the physiologic elastance or compliance of any specific part of the arterial system, E_a represents an "effective" arterial elastance as the ventricle ejects. Therefore E_a suits the assessment of the effect of IABP in the in situ heart. When the ventricle is coupled with the arterial system, the equilibrium is determined graphically as the intersection between the arterial and ventricular end-systolic pressure-volume relationships. In this framework, end-systolic volume is given as the intersection of these 2 lines, and stroke volume is the difference between the end-diastolic and end-systolic volumes.

Statistics. Comparisons of variables among the groups were tested by 2-tailed paired *t* test. Data are presented as mean ± SD unless otherwise indicated.

Result

Fig 3 shows the pressure-volume loop and the end-systolic pressure-volume relationship in the control and heart failure runs. Acute ischemic heart failure reduced E_{max} from 2.9 to 1.8 mm Hg · mL · 100 g LV weight^{-1} and resulted in the significant rightward shift of the pressure-volume loop. However, in both runs, IABP did not affect E_{max} itself. In the control run, although IABP reduced the peak LV pressure and changed the shape of the pressure-volume loop, the effect on the end-systolic pressure-volume data was minimal. On the other hand, IABP in heart failure significantly affected both end-systole and end-diastole, which resulted in a significant leftward shift of the pressure-volume loop. As a result, end-systolic pressure decreased from 86 to 80 mm Hg. Stroke volume increased from 13.7 to 15.9 mL. Effective E_a reduced from 6.3 to 5.5 mm Hg · mL · 100 g LV weight^{-1}. The ratio, E_a/E_{max}, reduced from 3.5 to 2.9.

Table I averages hemodynamic parameters in the control and heart failure model. The heart rate did not change during the experiment. Because we administered whole blood to maintain systemic arterial pressure, both end-systolic volume and end-diastolic volume increased by 76% ± 35% and 44% ± 23%, respectively. Hence, although end-systolic pressure did

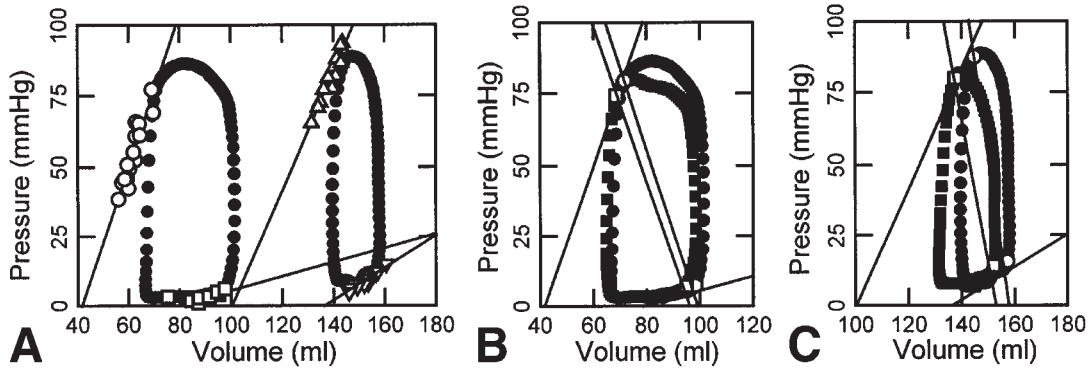

Fig 3. Pressure-volume relationships in the control and heart failure runs. **A**, Pressure-volume loop shifted to the left with the reduction of the slope of the end-systolic pressure-volume relationship and the increases in volume intercept after microsphere injection. *Open circles* and *triangles* represent end-systolic pressure-volume data points during inferior vena cava occlusion. **B**, Pressure-volume loops of the control run. *Closed squares* represent the pressure-volume loop without IABP; *circles* represent the pressure-volume loop with IABP. **C**, Heart failure run. *Open circles* and *squares* represent the end-systolic and end-diastolic pressure-volume data.

Table I. *Hemodynamic parameters during heart failure induction*

	Control	*Control IABP*	*P vs control*	*Heart failure*	*P vs control*	*Heart failure IABP*	*P vs heart failure*
HR (beats/min)	97 ± 18	97 ± 16	.932	94 ± 15	.544	91 ± 13	.128
EDV (mL)	101 ± 34	102 ± 34	.670	143 ± 36*	<.001	137 ± 36*	.008
ESV (mL)	72 ± 27	70 ± 26	.164	122 ± 35*	<.001	114 ± 34*	.002
SV (mL)	30 ± 11	32 ± 13	.064	21 ± 6*	.008	24 ± 6†	.036
EDP (mm Hg)	10.3 ± 4.1	9.9 ± 5.0	.572	14.1 ± 3.4*	.003	12.8 ± 3.5	.014†
ESP (mm Hg)	63 ± 16	64 ± 18	.602	68 ± 16	.155	62 ± 16*	.001
CVP (mm Hg)	5.4 ± 2.0	5.4 ± 1.7	.999	8.2 ± 2.6*	<.001	7.8 ± 2.3	.220
mAoP (mm Hg)	57 ± 16	63 ± 17*	.004	57 ± 16	.782	61 ± 14†	.014

Values are given as mean ± SD. *HR*, Heart rate; *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *SV*, stroke volume; *EDP*, end-diastolic pressure; *ESP*, end-systolic pressure; *CVP*, central venous pressure; *mAoP*, mean aortic pressure.
*$P < .01$, compared with the control run.
†$P < .05$, compared with the control run.

not significantly change, stroke volume decreased by 22% ± 28%. IABP increased mean aortic pressure in both the control and heart failure runs. However, IABP did not affect these hemodynamic parameters in the controls. On the other hand, during heart failure, IABP increased stroke volume by 15% ± 18% with decreases in end-systolic pressure. IABP also decreased end-diastolic pressure and volume 3% ± 5% and 9% ± 11%, respectively, which indicates that preload of the LV is also reduced although stroke volume increased.

Fig 4 averages the parameters for LV mechanics and the E_a in all 12 animals. Contractility after microsphere injection was shown by E_{max} (decreased from 2.7 ± 0.5 mm Hg to 1.3 ± 0.4 mm Hg · mL^{-1} · 100 g LV^{-1}). IABP did not change E_{max} (2.7 ± 0.5 mm Hg to 2.9 ± 0.7 mm Hg · mL^{-1} · 100 g LV^{-1} control versus 1.3 ± 0.4 mm Hg to 1.3 ± 0.5 mm Hg · mL^{-1} · 100 g LV^{-1} heart failure). However, IABP significantly decreased E_a in heart failure (2.5 ± 1.3 mm Hg to 2.6 ± 1.6 mm Hg · mL^{-1} · 100 g LV^{-1} in the controls versus 3.6 ± 1.3 mm Hg to 2.9 ± 1.2 mm Hg · mL^{-1} · 100 g LV^{-1} heart failure). As a result, the ratio, E_a/E_{max} decreased from 3.1 ± 0.8 to 2.3 ± 0.8. Although pressure-volume area did not change in the controls, in heart failure, pressure-volume area decreased from 951 ± 288 mm Hg · mL · 100 g LV $weight^{-1}$ to 862 ± 269 mm Hg · mL · 100 g LV $weight^{-1}$; EW did not change. When work efficiency was assessed by the ratio, EW/pressure-volume area (EW/PVA) improved from 46% ± 6% to 53% ± 7%. This suggested the improvement of the mechanical efficiency from myocardial oxygen consumption to EW as the improved E_a/E_{max} ratio suggested.

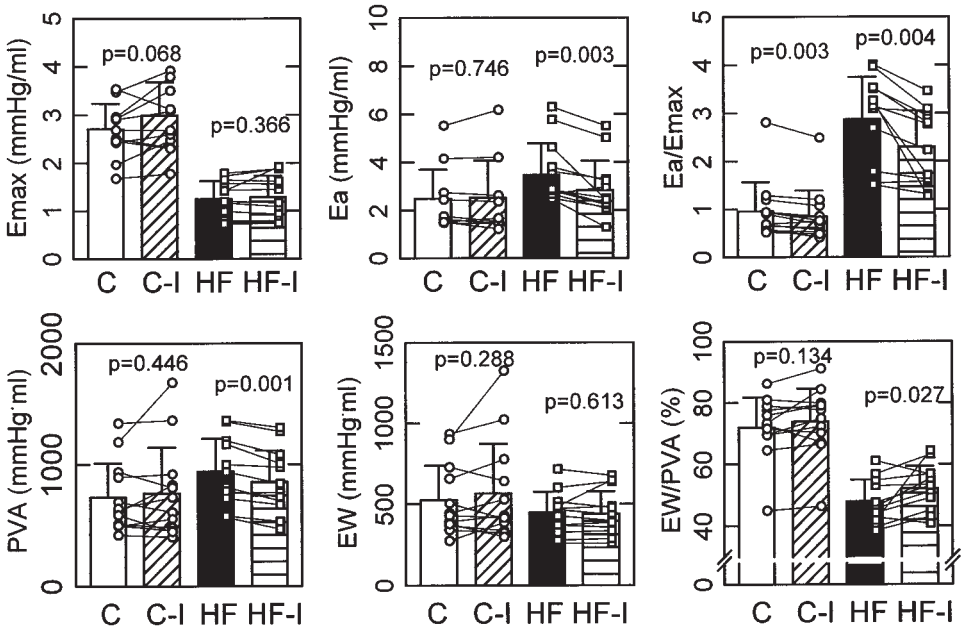

Fig 4. Left ventricular mechanics and ventriculoarterial coupling. *Circles* and *squares* indicate the individual data. Comparison of left ventricular mechanics and ventriculoarterial coupling with IABP. Means ± SD indicated. *C*, Control; *C-I*, control with IABP; *HF*, heart failure; *HF-I*, heart failure with IABP.

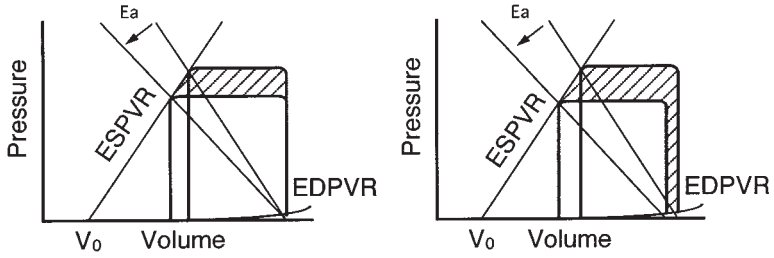

Fig 5. Schematic diagram of changes in pressure-volume loops with IABP. IABP induced changes in E_a (*arrows*). *Shadowed areas* represent the pressure-volume area preserved when the pressure-volume loop changed by IABP. Reduction of the pressure-volume area is larger with the preload reduction (*shaded area*). *ESPVR*, End-systolic pressure-volume relationship; *EDPVR*, end-diastolic pressure-volume relationship.

Discussion

The mechanism of IABP for cardiac support has been recognized as a reduction of LV work load achieved by afterload reduction[1,2] and an enhancement of coronary blood flow secondary to a diastolic augmentation.[3] This would result in an improvement of oxygen supply/demand ratio of the heart. Therefore IABP has been recognized to have an important role in the treatment of the patient with acute heart failure. However, the effect of IABP on LV mechanics assessed with the ventricular elastance, E_{max}, and/or arterial elastance, E_a, is limited.[20]

Bavaria and colleagues[20] assessed E_{max} with circulatory assist devices on stunned myocardium. Despite a similar leftward shift of the pressure-volume loop, they observed a significant increase in E_{max} with IABP although we found no improvements. This may depend on the difference of the coronary perfusion pressure. In our experiment, "mean" aortic pressure was maintained at 57 ± 16 mm Hg to maintain the coronary perfusion although LV "peak" pressure was 57 ± 12 mm Hg in their experiment.[20] Therefore there is a possibility that the coronary perfusion pressure was not high enough to maintain coronary blood flow, which would result in deterioration of LV contractility, E_{max}. E_{max} is more coronary perfusion pressure dependent when perfusion pressure becomes less than 50 mm Hg.[21] When the coronary perfusion pressure is maintained above the physiologic

range where coronary autoregulation exists, LV contractility may not necessarily be enhanced by IABP.

The effect of IABP on LV mechanics is well understood when E_a is taken into account.[17-19] The artery is characterized as an elastic chamber with a volume elastance, similar to the ventricle, which has the end-systolic pressure-volume relationship. The coupling between the ventricle and arterial afterload is characterized in terms of the slope of the end-systolic pressure-volume relationship, E_{max}, and the slope of the arterial end-systolic pressure-stroke volume relationship, E_a.[19] Both of these relationships are superimposed in the same pressure-volume plane where the stroke volume that the ventricle can eject from a given end-diastolic volume is represented as the intersection of these 2 relationships. IABP decreased E_a, which suggested reduction of aortic impedance especially in heart failure.[2] When E_a decreases without affecting E_{max}, the intersection point shifts down and to the left, resulting in an increase in stroke volume as shown in Fig 5, *A*. This has been considered one of the major mechanisms to increase stroke volume with afterload reduction.[22]

The ventricle transfers the mechanical energy of contraction to the intracavitary blood as an adequate flow to the arterial system. When the energy source and its load are matched, a maximal amount of energy is transferred from the source to the load.[l8] This is important because, for any given state of preload, contractility, and afterload, there is a unique combination of ventricular and arterial elastances that will maximize ventricular stroke work, or EW.[17,18] The optimality of afterload is defined as the ratio of EW to its maximal value (appendix).[23]

Over 1.0 of E_a/E_{max}, the optimality proportionally decreases as E_a/E_{max} increases (Fig 6). Ratios outside of the range of 0.5 to 1.0 are said to reflect varying degrees of ventriculoarterial uncoupling and changes in the ratio of E_a to ventricular contractility. The deterioration of the optimality in the ventricle with poor contractility has been demonstrated in animals and in patients.[24,25] In our experiment, the significant reduction (Fig 6) of optimality suggested severe uncoupling after heart failure induction.[26] To improve the optimality, enhancement of E_{max} and/or reduction of E_a is necessary. Our result showed that IABP effectively reduces E_a without affecting E_{max} and improving E_a/E_{max}. The afterload reduction with other methods would result in the decrease of the end-systolic pressure and hence mean pressure, which is disadvantageous to maintain coronary perfusion pressure. On the other hand, with diastolic augmentation, IABP improves the relationship by reducing E_a without compromising coronary perfusion pressure. By changing the E_a/E_{max} ratio to the normal side, IABP improves afterload particularly in heart failure by decreasing myocardial oxygen consumption and/or increasing EW.

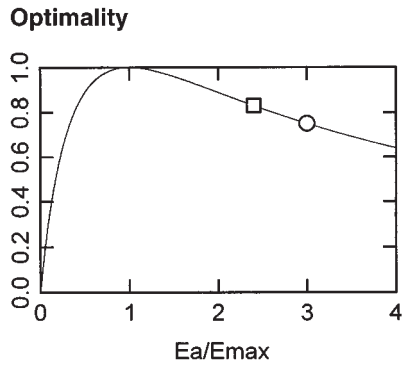

Fig 6. Changes in the optimality of the afterload with IABP after heart failure as a function of the ventriculoarterial ratio, E_a/E_{max}. The optimality of the afterload becomes unity when E_a/E_{max} is unity. When E_a/E_{max} changes from 3.0 to 2.4, the optimality increases from 0.75 to 0.83. The *open square* indicates the average data for the heart failure with IABP. The *open circle* indicates the average data for the heart failure.

In addition, our data suggested that IABP also has the unloading effect of the LV as shown in reduced end-diastolic volume and pressure. As IABP reduced preload and afterload of the heart in the heart failure run, it resulted in the significant reduction of pressure-volume area. Fig 5, *B*, shows the schematic diagram of pressure-volume loops with the preload reduction. With decrease in end-diastolic volume, the intersection between the ventricular and arterial end-systolic pressure-volume relationship further shifts to the left. Therefore, with a given change in E_a as shown, the reduction of the pressure-volume area is much greater with the preload reduction. As pressure-volume area linearly correlates with myocardial oxygen consumption, our result suggests that IABP has the effect of myocardial oxygen conservation because of the preload reduction, especially in the damaged heart.

Despite the significant increase in stroke volume with IABP in heart failure, IABP did not increase EW, which is presumably due to the afterload reduction. However, it resulted in a significant reduction in potential energy and pressure-volume area. Because of the reduction of pressure-volume area with unchanged EW, there is a significant improvement in work efficiency of the heart. Work efficiency does not change with mechanical efficiency (EW/myocardial oxygen consumption) in a parallel manner because mechanical efficiency is the product of work efficiency and efficiency from myocardial oxygen consumption to pressure-volume area. However, this suggests the possibility

that mechanical efficiency is effectively improved with the preload reduction and the correction of the ventriculoarterial coupling toward the normal side although mechanical efficiency might not improve to the same extent as work efficiency improved.

The same extent of changes in ventriculoarterial coupling in vasodilator therapy has been observed in the heart failure patient.[16] Others have measured the same parameters (such as E_{max}, E_a, E_a/E_{max}, EW/PVA) and concluded that the reduction of afterload with nitroprusside plays an important role in restoring optimal ventricular load, in which work efficiency is improved by changing the ratio, E_a/E_{max}. Therefore the reduction of end-diastolic volume, E_a/E_{max}, and improvement of work efficiency is consistent with afterload reduction regardless of the mechanism to reduce the afterload.

The primary limitation of this study that could affect its applicability to clinical IABP is that we used a microsphere-induced heart failure model. In the patients with postcardiotomy after coronary artery bypass graft, the damage to the heart may be different from our model even though the hemodynamic change is similar. The conservation of myocardial oxygen consumption with IABP is strongly suggested from the pressure-volume diagram. In addition, although pressure-volume area linearly correlates with myocardial oxygen consumption, EW/PVA does not always represent the changes in the mechanical efficiency when the relation between pressure-volume area and myocardial oxygen consumption changes with the intervention. Because we did not measure myocardial oxygen consumption, the direct measurement of myocardial oxygen consumption will be necessary to characterize fully the effect of IABP on LV energetics.

To calculate the optimality, we used the same equation as Sunagawa's group.[22] They ignored the diastolic compliance on EW area to simplify the equation. However, especially in heart failure, this part may not be small enough to be negligible. In that case, the optimal relationship becomes preload dependent of the LV because the diastolic compliance is exponentially preload dependent. Therefore the optimal relationship might not improve to the same extent as shown in this article.

In conclusion, IABP unloads the LV by reducing preload and afterload especially in the failing heart. IABP decreases afterload by improving ventriculoarterial coupling. Data suggested that IABP improves mechanical efficiency of the LV.

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Appendix

On the pressure-volume diagram, end-systolic pressure, Pes, is determined with either E_{max} or E_a as follows:

$$Pes = E_{max} \times (Ves - V_0)$$

$$Pes = -E_a \times (Ves - Ved)$$

where Ves and Ved are end-systolic and end-diastolic volume, respectively. Then, end-systolic volume is calculated as:

$$Ves = \frac{E_a \times (Ved - V_0)}{E_{max} + E_a}$$

Because stroke volume is calculated as (Ved – Ves), assuming a constant LV pressure during ejection, EW is approximated as:

$$EW \approx \text{stroke volume} \times Pes = (Ved - Ves) \times Pes =$$

$$\left[Ved - \frac{E_a \times (Ved - V_0)}{E_{max} + E_a}\right] \times \frac{E_{max} \times E_a \times (Ved - V_0)}{E_{max} + E_a} =$$

$$\frac{E_a \times (Ved - V_0)^2}{(1 + E_a/E_{max})^2} = E_{max} \times (Ved - V_0)^2 \times \frac{E_a/E_{max}}{(1 + E_a/E_{max})^2}$$

Therefore EW is a function of E_{max} and E_a. From Equation 1, maximal EW (EW_{max}) will be obtained when E_{max} equals E_a:

$$EW_{max} = \frac{E_{max}}{4} (Ved - V_0)^2 = 4 \times \frac{E_a/E_{max}}{(1 + E_a/E_{max})^2} = \frac{4E_aE_{max}}{(E_{max} + E_a)^2}$$

Then maximal EW generated by the ventricle is determined by the ratio E_a/E_{max} as shown in Fig 6. The optimal ratio is achieved when the E_a/E_{max} is 1.[23]