Efficiency of energy transfer from pressure-volume area to external mechanical work increases with contractile state and decreases with afterload in the left ventricle of the anesthetized closed-chest dog

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ABSTRACT We studied the effects of ventricular end-systolic elastance (Ees) and effective arterial elastance (Ea) on the efficiency of energy transfer from pressure-volume area (PVA) to external mechanical work (EW) in the left ventricle of anesthetized closed-chest dogs. PVA represents the total mechanical energy generated by ventricular contraction, which is an intermediate form of energy between oxygen consumption, the total energy input, and EW, the effective energy output. PVA and EW were determined from ventricular pressure and volume, which were continuously measured with a volumetric conductance catheter. Measurements of Ees were obtained by transiently increasing afterload by an inflation of a Fogarty catheter in the thoracic descending aorta. Ea was determined as the ratio of end-systolic pressure to stroke volume. The EW/PVA efficiency of a steady-state contraction increased from 55% to 64%, with a 58% increase in Ees after dobutamine. Ees, which was smaller than Ea before dobutamine, became nearly equal to Ea after dobutamine, maximizing EW for a given end-diastolic volume. EW/PVA efficiency decreased with an abrupt increase in afterload before and after dobutamine. The sensitivity of the decrease in the EW/PVA efficiency to an increase in end-systolic pressure was significantly less after than before dobutamine. We could account for all these changes in EW/PVA efficiency by the relative changes in Ees and Ea in the pressure-volume diagram.
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MECHANICAL EFFICIENCY of the heart as the ratio of external mechanical work (EW) to myocardial oxygen consumption (VO_2) varies between 0 and 30% as a function of ventricular loading conditions and contractile state.[1–4] We have recently found that this efficiency can be divided into two steps: the efficiency of energy transfer from VO_2 to pressure-volume area (PVA) as the first step, and the efficiency of energy transfer from PVA to EW as the second step,[4–6] as shown in figure 1, *A*. PVA, which represents the total mechanical energy generated by ventricular contraction, is an intermediate form of energy between the first and second steps.[4–6] PVA is defined as the area circumscribed by the end-systolic and end-diastolic pressure-volume relations and the systolic pressure-volume trajectory, as shown in the diagram[5–8] in figure 1, *B*.

We have already extensively studied the efficiency of energy transfer from VO_2 to PVA and found it a function of loading conditions and contractile state in excised hearts as well as hearts in situ.[6–8] The load- and contractility-dependent overall efficiency from VO_2 to EW could be better understood by the quantitative study of the efficiency of energy transfer from PVA to EW as a function of afterload and contractile state.

In this study we wanted to determine whether we could theoretically predict the changes in EW/PVA efficiency when contractility and afterload were altered. The theoretical predictability of this efficiency would greatly facilitate the quantitative understanding of the changes in cardiac mechanical efficiency under normal and pathologic conditions. To this end, we used a volumetric conductance catheter[9] to study in situ left ventricles of anesthetized closed-chest dogs, the feasibility of which has already been established.[10, 11] To analyze experimental results, we used Ees and Ea. Ees, end-systolic ventricular elastance, is the slope of the end-systolic pressure-volume relation (ESPVR),[12–14]

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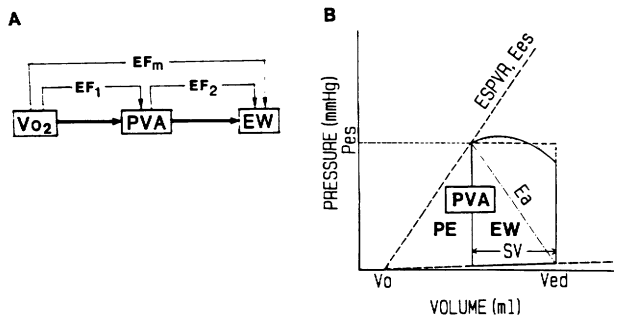

FIGURE 1. *A*, EF_m = the mechanical efficiency of energy transfer from VO_2 to EW; EF_1 = the efficiency from VO_2 to PVA; EF_2 = the efficiency from PVA to EW; $EF_m = EF_1 \cdot EF_2$. *B*, Schematic illustration of PVA. PVA is the area in the pressure-volume (P-V) diagram that is circumscribed by the ESPVR line, the end-diastolic pressure-volume relation (EDPVR) curve, and the systolic segment of pressure-volume trajectory (solid). PVA consists of the EW, which is the area under the systolic segment of the pressure-volume trajectory, and the elastic potential energy (PE) under the ESPVR line. Effective Ea is the ratio of end-systolic pressure (Pes) to stroke volume (SV). Ved = end-diastolic volume. The dashed line simulates constant ejection pressure equal to Pes. Dotted area shows the difference between experimentally obtained EW and EW calculated in the simulation.

as shown in figure 1, *B*, and Ea, effective arterial elastance, is the ratio of end-systolic pressure to stroke volume,[15, 16] as shown in figure 1, *B*. The combination of Ees and Ea has been proven a powerful tool for quantitative understanding of cardiac mechanics and its interaction with afterload.[15–17]

Methods

Preparation. Seven mongrel dogs weighing 12 to 17 kg were anesthetized with ketamine hydrochloride (5 mg/kg im) followed by intravenous sodium pentobarbital (25 mg/kg) without any additional dose of the anesthetics over the course (0.5 to 1 hr) of each experiment. Each dog was artificially ventilated through an endotracheal tube with a positive-pressure respirator (SN-480-3, Shinano, Japan).

Left ventricular pressure was monitored with a micromanometer-tipped catheter with a fluid-filled lumen (Millar Instruments, PC-470) passed retrograde from the carotid artery. An eight-electrode volumetric conductance catheter (Cordis Europa NV, Roden, The Netherlands) was inserted into the left ventricle from the carotid artery with the help of a homemade polyethylene introducer sheath. A No. 7F Swan-Ganz catheter was inserted into the external jugular vein and advanced to the pulmonary artery to determine the correction volume deriving from the parallel conductance of all structures surrounding the left ventricular cavity.[9] A catheter was placed in the femoral vein for blood sampling to determine the specific resistivity of blood. A Fogarty catheter (Edwards Laboratories, Model 32-080-8/10F) was inserted into the thoracic descending aorta from the femoral artery and was transiently (2 to 5 sec) inflated with 3 to 7 ml of water for determination of ESPVR and to produce transient increases in afterload.

Volume measurement. We connected the volumetric catheter to a volumetric system (Model Sigma 5, Leycom, Oegstgeest, The Netherlands) to measure left ventricular conductance and convert it to left ventricular volume.[9, 11] The catheter had eight electrodes spaced at 1 cm intervals and was excited by an alternating current (30 μA, 20 kHz) across the distal and proximal electrodes. We monitored the segmental volume signals from the other six electrodes on an oscilloscope according to the Sigma 5 Users Manual. The final position of the catheter in the left ventricle, with the most distal electrode placed near the apex and the most proximal electrode just cephalad to the aortic valve, was chosen according to the manual. The position was confirmed on postmortem examination.

The Sigma 5 instantaneously obtained left ventricular volume [V(t)] by:

$$V(t) = (1/\alpha)\cdot L^2\cdot\rho\cdot G(t)\ \ Vc \qquad (1)$$

where G(t) is the sum of the segmental conductances, L is interelectrode distance, and α is an empirical slope coefficient for the V(t)-G(t) correlationship. α is assumed to be 1.0 by the Sigma 5. Vc is the correction volume for the parallel conductance. To obtain V(t), we had to determine correction volume from the conductance signals recorded after an injection of hypertonic salt solution (10% NaCl) into the pulmonary artery. We used a signal-processing computer system (7T17, NEC San-Ei, Japan) and software that we developed to determine correction volume by the method described in the manual. ρ is the resistivity of blood and was measured in a resistivity cuvette attached to the Sigma 5.

Data analysis. The signals of the electrocardiogram (ECG), left ventricular pressure, and left ventricular volume were digitized at 3 msec intervals and analyzed with the 7T17. We analyzed the pressure-volume loops obtained within 3 sec after the initial increase in afterload pressure caused by inflation of the Fogarty catheter. An ESPVR line was drawn on the left upper corners of the pressure-volume loops of the last one or two steady-state contractions and the initial six to eight contractions (<3 sec) during the increase in afterload pressure. We obtained Ees as the slope of the ESPVR line and V_0 as the volume axis intercept to the ESPVR line. End-systolic pressure was identified as the pressure of the left upper corner of the pressure-volume trajectory. Left ventricular end-diastole was considered to lie in the right lower corner of each pressure-volume loop.

PVA was determined as the area under the ESPVR line and the systolic pressure-volume trajectory and above the end-diastolic pressure-volume relation (EDPVR) curve, as shown in figure 1, *B*. EW was determined as the area within the pressure-volume loop. Planimetry was done on hard copies of the pressure-volume trajectories with a digitizer (Model DT-1000, Graphtec, Japan) that was connected to a computer (PC-9801E, NEC, Japan). The dimensions of PVA and EW are millimeters of mercury per milliliter, which is the same as the dimensions of energy.

We determined the effective arterial elastance (Ea), as proposed by Sunagawa et al.,[15, 16] as the ratio of the end-systolic pressure (Pes) to stroke volume (SV). Thus,

$$Ea = Pes/SV \qquad (2)$$

Ea is the negative value of the slope (<0) of the diagonal line connecting the end-diastolic and end-systolic pressure-volume points of the pressure-volume trajectory. We changed Ea by increasing the afterload with the intra-aortic Fogarty catheter in a given contractile state.

Experiment protocol. Resistivity (ρ) of circulating blood was measured and its value was set in the Sigma 5 in each experiment. The correction volume was then determined. A 2 ml injection of hypertonic salt solution was repeated three times and the mean value for correction volume was determined in each experiment. Before the injection of hypertonic solution or the inflation of the Fogarty catheter, artificial ventilation was

stopped at the end of expiration for about 10 sec to eliminate respiration induced changes in hemodynamics.

Control run. A control study was performed in seven dogs. The Fogarty catheter was manually inflated with 3 to 7 ml saline. The inflation was repeated three times at intervals of 3 to 5 min.

Dobutamine run. After the control study, contractile state was enhanced by a continuous intravenous infusion of dobutamine at a rate of 5 to 10 μg/min/kg. As in the control study, the Fogarty catheter was inflated three times.

Statistics. Mean values are reported for all data (heart rate, V_0, stroke volume, end-systolic pressure, Ees, Ea, and the EW/ PVA efficiency) obtained during the three successive inflations of the Fogarty catheter in the control and dobutamine runs. Data from the control and dobutamine runs were compared by paired t test. p values smaller than .05 were considered indicative of a statistically significant difference. Data are presented as the mean ± SD.

Theoretical considerations. We examined theoretically whether the experimental results could be accounted for by the known pressure-volume relation of the ventricle.

We used the same mathematic formulas used previously to relate EW, PVA, and Ees[4, 8]:

$$EW = SV \cdot Pes \quad (3)$$

$$PVA = EW + 0.5\ Pes^2/Ees \quad (4)$$

where SV = stroke volume; Pes = end-systolic pressure. For simplicity, we assumed that ventricular pressure during ejection was equal to end-systolic pressure, as shown by the dashed line in figure 1, *B*. From equations 3 and 4:

$$EW/PVA = SV/(SV + 0.5\ Pes/Ees) \quad (5)$$

Ea can be approximated by equation 2. From equations 2 and 5:

$$EW/PVA = Ees/(Ees + 0.5\ Ea) = 1/(1 + 0.5\ Ea/Ees) \quad (6)$$

We tested the hypotheses that equation 5 or 6 could account for the experimental results.

Results

Mean values for the resistivity (ρ) of blood and the correction volume in seven dogs were 140 ± 21 Ω cm and 62.4 ± 12.2 ml, respectively. The coefficient of variation of correction volume in each experiment was 8.2 ± 3.6%.

Figure 2 illustrates representative examples of the pressure-volume loops and ESPVR lines obtained with transient increases in afterload in control and dobutamine runs in the same dog. Peak ventricular pressure increased by 30 to 40 mm Hg and residual volume

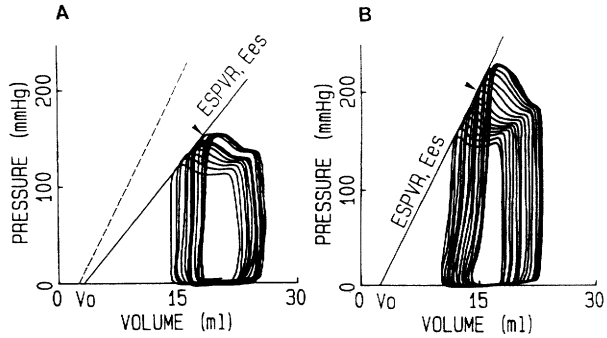

FIGURE 2. Representative pressure-volume trajectories and ESPVR lines (solid lines) during steady-state contractions (shortest loops) and under conditions of transiently increased afterload (growing loops) under control conditions (*A*) and with dobutamine-enhanced contractility (*B*). Arrows indicate the initial eight contractions that were analyzed during transiently increased afterload. Dashed line in *A* is the ESPVR line transcribed from *B*.

increased by 3 ml within the initial 8 beats during the increase in afterload pressure. The end-systolic pressure-volume points of steady-state contractions and the initial eight transient contractions were reasonably well fitted by the linear ESPVR. Thereafter, end-systolic pressure-volume points of transient contractions tended to deviate rightward from the linear ESPVR. We excluded these deviating contractions from the analysis. Dobutamine markedly increased Ees but changed V_0 little. Dobutamine decreased end-diastolic volume of the steady-state contraction (shortest loop).

We examined the reproducibility of Ees obtained during the three aortic occlusions repeated at intervals of 3 to 5 min. The coefficient of variation of Ees in each run was 0.08 ± 0.03. Table 1 shows the mean values during steady-state contractions for the control and dobutamine runs in all seven hearts. Dobutamine significantly increased heart rate and Ees ($p < .01$), and decreased V_0 in three of 7 dogs; in four dogs V_0 increased. The changes in V_0 were not significant on the average.

As shown in table 2, dobutamine significantly increased end-systolic pressure and effective Ea during steady-state contractions ($p < .01$). The drug did not significantly change stroke volume under these condi-

TABLE 1
Comparison of data obtained during control and dobutamine runs

Condition	HR (beats/min)	V_0 (ml)	Ees (mm Hg/ml)	Δ (EW/PVA)/ΔEa ($\times 10^{-2}$ ml/mm Hg)	Δ (EW/PVA)/ΔPes ($\times 10^{-3}$/mm Hg)
Control	187 ± 18	3.5 ± 3.2	8.9 ± 2.2	1.63 ± 0.64	3.17 ± 0.77
Dobutamine	204 ± 20[A]	1.7 ± 4.4[NS]	14.1 ± 3.5[A]	1.77 ± 0.82[NS]	1.77 ± 0.64[A]

HR = heart rate; Pes = end-systolic pressure.
[A]$p < .01$.

TABLE 2

Comparison of data obtained at steady state and during transiently increased afterload and of control and dobutamine data

Condition	SV (ml)	Pes (mm Hg)	Ea (mm Hg/ml)	Ea/Ees dimensionless)	EW/PVA (%)
Control					
S	11.2 ± 3.2	142 ± 14	13.4 ± 3.5	1.49 ± 0.26	55.4 ± 5.4
A	8.8 ± 2.4[A]	187 ± 29[A]	21.7 ± 6.4[A]	2.42 ± 0.45[A]	41.2 ± 7.3[A]
Dobutamine					
S	11.3 ± 3.1[NS]	161 ± 14[B]	15.1 ± 3.6[B]	1.08 ± 0.23[B]	64.0 ± 4.5[B]
A	10.7 ± 2.6[NS]	208 ± 18[A]	20.9 ± 7.7[A]	1.50 ± 0.45[A]	58.0 ± 7.6[A]

S = steady state before increasing afterload; A = transiently increased afterload; SV = stroke volume; Pes = end-systolic pressure.

[A]$p < .01$ compared with steady state; [B]$p < .01$ compared with control run.

tions, but Ea/Ees was decreased from 1.49 ± 0.26 (dimensionless) to 1.08 ± 0.23 ($p < .01$).

After a transient increase in afterload, stroke volume significantly decreased during the control run ($p < .01$), but did not significantly decrease during the dobutamine run. The increase in afterload significantly increased both Ea and Ea/Ees in both runs ($p < .01$).

Dobutamine increased EW/PVA efficiency during the steady-state contractions from 55.4 ± 5.4% to 64.0 ± 4.5% ($p < .01$), as shown in table 2. The increase in afterload significantly decreased EW/PVA efficiency in both runs ($p < .01$).

Figure 3, *A*, shows the scatter diagram of EW/PVA efficiency against Ees of the steady-state contractions in the control and dobutamine runs in all seven dogs. We found a positive correlation between the EW/PVA efficiency and Ees, with a correlation coefficient of .55 ($p < .05$). This correlation supports the increased EW/PVA efficiency with dobutamine shown in table 2.

Figure 3, *B*, shows the theoretical predictions made by equation 5 at five different cardiac output levels between 1.0 and 3.0 liters/min at a constant heart rate of 190 beats/min and a constant end-systolic pressure of 150 mm Hg. In fact, cardiac output was between 1.2 and 3.0 liters/min under steady-state conditions in the dogs in our study. The EW/PVA efficiency increased logarithmically with increases in Ees. The experimental data in Figure 3, *A*, reasonably resemble the slow rising portion of the prediction curves. Both experimentally and theoretically, EW/PVA efficiency only increased from 40% to 50%, to 70% to 80%, with the increases in Ees from 7 to 21 mm Hg/ml.

Figure 4, *A*, shows decreases in EW/PVA efficiency with increases in Ea caused by the increase in afterload

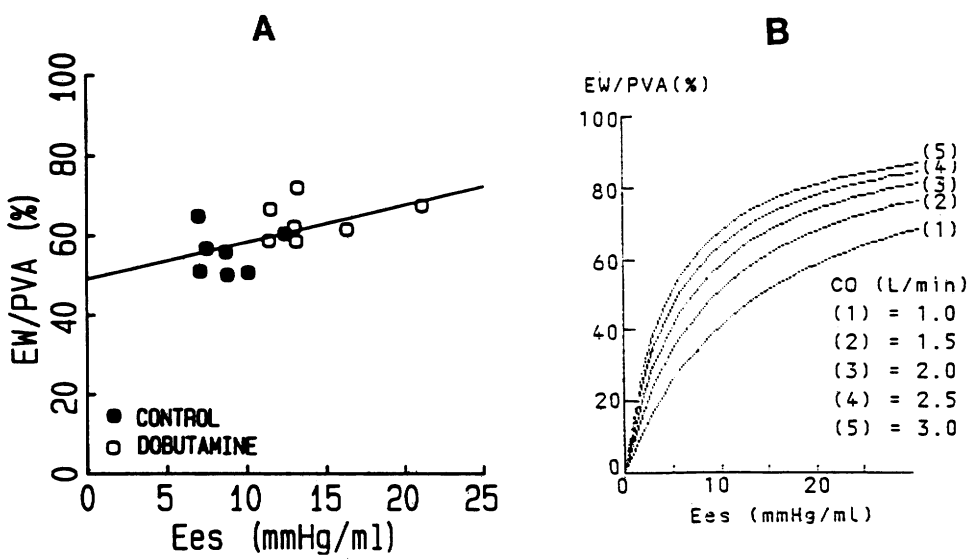

FIGURE 3. *A*, Regression of the EW/PVA efficiency on Ees during steady-state contractions regardless of contractile state. Closed circles represent control data and open circles data obtained during dobutamine enhanced contractile state. The solid line is the linear regression line. *B*, Simulation of the relation between EW/PVA efficiency and Ees at five different cardiac output levels. We assumed that heart rate was constant at 190 beats/min and end-systolic pressure was constant at 150 mm Hg.

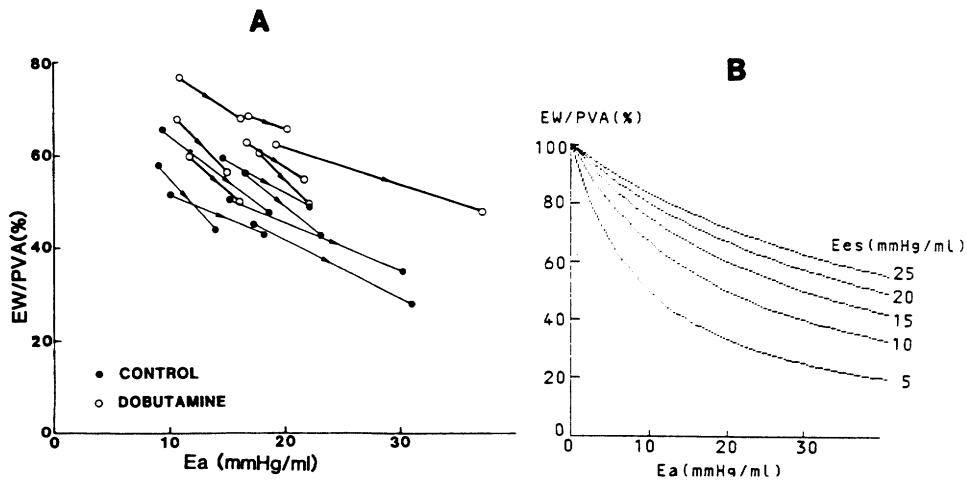

FIGURE 4. *A,* Relation between EW/PVA efficiency and the effective Ea in a steady-state contraction and in the initial six to eight contractions during transiently increased afterload. Arrows indicate the direction of changes in values from steady state to increased afterload. Closed circles represent the control data and open circles data obtained during the dobutamine-enhanced contractile state. *B,* Simulation of the relation between EW/PVA efficiency and Ea at five different Ees levels. See text for details.

during the control and dobutamine runs. The slope of the line relating the decrease in the EW/PVA efficiency to the increase in Ea [Δ(EW/PVA)/ΔEa in table 1] caused by this increase in afterload was 0.016 ± 0.006 ml/mm Hg in the control run and 0.018 ± 0.008 ml/mm Hg in the dobutamine run (NS, table 1). This finding indicates that the sensitivity of EW/PVA efficiency to a change in afterload in terms of Ea was the same in both the control and dobutamine runs.

Figure 4, *B*, shows theoretical predictions made by equation 6 at five different Ees levels. The EW/PVA efficiency decreased with the increase in Ea and increased with the increase in Ees. The sensitivity of the decrease in the EW/PVA efficiency to an increase in Ea of between 10 and 30 mm Hg/ml was almost the same for different Ees values. The experimental data in figure 4, *A*, agree reasonably well this prediction.

Figure 5, *A*, illustrates the decreases in EW/PVA efficiency with increases in end-systolic pressure under conditions of transiently increased afterload in the control and dobutamine runs. The slope of the line relating the decrease in EW/PVA efficiency to the increase in Pes [Δ (EW/PVA)/Δ Pes in table 1] caused by the increased afterload was $3.17 \times 10^{-3} \pm 0.77 \times 10^{-3}$/mm Hg in the control runs and $1.75 \times 10^{-3} \pm 0.63 \times 10^{-3}$/mm Hg in the dobutamine run. The slope

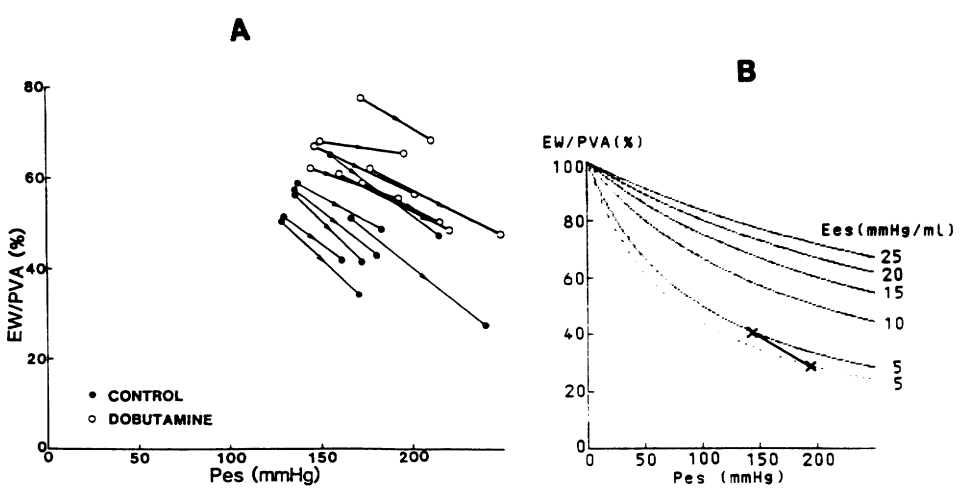

FIGURE 5. *A,* Relation between EW/PVA efficiency and end-systolic pressure (Pes) in a steady-state contraction and in the initial six to eight contractions during transiently increased afterload. Arrows indicate the direction of changes in values from steady state to increased afterload. Closed circles represent control data and open circles data obtained during the dobutamine-enhanced contractile state. *B,* Simulation of the relation between EW/PVA efficiency and Pes. Solid curves are at five different Ees levels and a constant stroke volume of 10 ml. Dashed curve is at Ees of 5 mm Hg/ml and stroke volume of 8 ml. The solid line connects a point (x) at which stroke volume is 10 ml and Pes is 140 mm Hg on the solid curve to a point (x) at which stroke volume is 8 ml and Pes is 190 mm Hg on the dashed curve at Ees of 5 mm Hg/ml. See text for details.

was significantly smaller in the dobutamine run than in the control run ($p<.01$), as shown in table 1. This finding indicates that the sensitivity of the EW/PVA efficiency to an afterload change in terms of end-systolic pressure was smaller in the enhanced contractile state.

Figure 5, *B*, shows the theoretical predictions made by equation 5 at five different Ees levels at a constant stroke volume of 10 ml. EW/PVA efficiency decreased with the increase in end-systolic pressure and increased with the increase in Ees (table 1). The sensitivity of the decrease in EW/PVA efficiency to an increase in end-systolic pressure of between 120 and 250 mm Hg was greater at a lower than at a higher Ees. Moreover, we simulated the greater sensitivity of the decrease in EW/PVA efficiency to end-systolic pressure at a lower Ees by incorporating the decreased stroke volume at a lower Ees, since EW/PVA is a function of both stroke volume and end-systolic pressure/Ees, as shown in equation 5. Stroke volume significantly decreased (22%) by transiently increased afterload in the control run, whereas it did not significantly decrease (6%) in the dobutamine run (table 1). The solid curves in figure 5, *B*, were obtained at a constant stroke volume of 10 ml. We then drew an additional prediction curve (dashed) for a Ees of 5 mm Hg/ml with a stroke volume of 8 ml, which is 20% smaller than the stroke volume set for the other curves. When a point was shifted from the solid curve for Ees of 5 mm Hg/ml and stroke volume of 10 ml to the new dashed curve for Ees of 5 mm Hg/ml and stroke volume of 8 ml while end-systolic pressure was increased from 140 to 190 mm Hg, the slope of this composite line was much steeper than the slope of the curve for Ees of 20 mm Hg/ml, as shown in figure 5, *B*. Thus, incorporation of the stroke volume change enabled us to simulate the experimental results.

Discussion

We have examined the effects of changes in left ventricular Ees and effective Ea on EW/PVA efficiency in the closed-chest anesthetized dogs with use of the volumetric conductance catheter. There were two important findings. First, enhanced ventricular contractility by dobutamine increased Ees and made Ees equal to Ea. This condition is known to maximize EW from a given end-diastolic volume[15, 16] and increases EW/PVA efficiency during steady-state contractions, as explained later. Second, the sensitivity of a decrease in EW/PVA efficiency to an increase in end-systolic pressure was significantly smaller in the enhanced contractile state, although the sensitivity of the decrease in EW/PVA efficiency to an increase in Ea was not significantly different under control conditions and enhanced contractile state. These two findings are conceptually supported by the data on Ees and Ea obtained in the simulation.

With regard to the assumptions necessary in the interpretation of our findings, we assumed that the conductance catheter could reliably measure left ventricular volume when it is abruptly changed over several beats under conditions of aortic occlusion.[9–11] The ESPVR curves obtained under steady-state conditions and during six to eight transient contractions (<3 sec) were reasonably linear and similar to those measured with a servo pump in an excised heart preparation.[11] Although blood probably pooled gradually in the pulmonary circulation and the right ventricle during aortic occlusion, the amount of blood pooled within the initial six to eight transient contractions was probably too small to affect the parallel conductance correction volume and hence the slope of the ESPVR.

Second, we assumed that we could minimize the baroreceptor reflex effects on ESPVR and Ees by examining only the initial several contractions (<3 sec) after each aortic occlusion despite the intact reflexes, although ventricular contractility may have been affected by the reflexes during the inflation of the Fogarty catheter. Since pharmacologic agents that block the reflexes generally have a negative inotropic effect, we did not administer any pharmacologic blockers. Although end-systolic pressure increased transiently by about 50 mm Hg in the present study, left ventricular Ees would decrease by 15% at most as a result of baroreceptor reflexes.[14] Moreover, cardiac responses to sympathetic nerve activity seem to have a latency of more than 2 sec,[18] and a time constant of at least 30 sec.[19, 20] The linear ESPVR within the initial six to eight transient contractions and apparent deviation of end-systolic pressure-volume points of later contractions from the linear ESPVR seem to support the validity of our assumption. Moreover, the degree of bradycardia that could occur as a result of reflex activity was 15 ± 7 msec in terms of the cardiac cycle period, supporting minimal involvement of baroreceptor reflexes.

Third, ESPVR may not be completely independent of changes in afterload.[21, 22] The ESPVR line slightly shifts to the left without the changes in Ees when afterload resistance increases.[21] This effect could slightly shift ESPVR during transiently increased afterload. However, we had no means to evaluate the effect of transient increase in afterload on ESPVR in the present study. We therefore assumed that ESPVR was

for practical purposes independent of end-systolic pressure and Ea in this study.

Fourth, we assumed in the simulation that ventricular pressure during ejection was equal to end-systolic pressure, as shown in figure 1, *B*. Therefore, EW, as assessed by equation 3, was subject to an error equal to the area (dotted in figure 1, *B*), between the actual pressure-volume trajectory and the horizontal end-systolic pressure level line during ejection. However, this area was only 8.1 ± 2.7% of SV·end-systolic pressure in this study. We therefore believe that the magnitude of this error in EW did not have serious effect on the simulation and its conclusion.

Fifth, since sodium pentobarbital depresses ventricular contractile state,[23] Ees in the present study may have also been somewhat depressed. The depressed Ees was raised by dobutamine. The range (7 to 21 mm Hg/ml) of the observed Ees values (figure 3, *A*) covers the values reported under different experimental conditions ranging from excised hearts to intact hearts in situ. We would therefore expect that the experimental results obtained are representative of a wide range of contractile states.

Finally, since the standard deviation of correction volume was 5.2 ± 2.7 ml in each experiment and V_0 was determined relative to the mean of three correction volume values, the variation in correction volume did not guarantee the accuracy of the absolute value for V_0. Changes in left ventricular volume relative to V_0 were not affected by correction volume. Therefore, the variation in correction volume did not reduce the accuracy of measurements of Ees, Ea, PVA, or EW in this study. One interesting result was that dobutamine increased Ees by 60% but did not consistently change V_0, inconsistent with previous studies.[24–26] This difference may be attributed in part to differences in the preparations (i.e., open-chest dogs in the previous studies[24, 25] vs closed-chest dogs in the present study), and in part to differences in the methods of generation of rapid loading changes (i.e., the transient inferior vena caval occlusion in the previous studies[24–26] vs the transient occlusion of the thoracic descending aorta in the present study). Further analysis of this difference is beyond the scope of this study.

Under the assumptions that have been discussed above, the consistency of the present experimental results of the EW/PVA efficiency with the theoretical prediction by the function of Ees, Ea, and end-systolic pressure, as shown in figures 3, *B*, 4, *B*, and 5, *B*, indicates that the observed results can reasonably be accounted for by the concept graphically shown in figure 6, which illustrates the pressure-volume loops, ESPVR lines, and Ea lines in scale that we observed under the three different conditions. Figure 6, *A*, shows loops during steady-state contractions in the control and dobutamine runs before the transient increase in afterload. Ea was greater than Ees in the control run, whereas Ea was almost equal to Ees in the dobutamine run (table 2). Since EW for a given end-diastolic volume is maximal when Ees is equal to Ea,[15, 16] dobutamine seems to have produced an energetically optimal coupling between the left ventricle and the arterial system, allowing maximal EW for a given end-diastolic volume and increasing EW/PVA efficiency.

Figure 6, *B* and *C*, illustrates the pressure-volume loops before and after a transient increase in afterload in the control and dobutamine runs. Ea markedly increased and became much greater than Ees in both runs (table 2). In contrast to the enhancement of contractility, the transient increase in afterload produced an

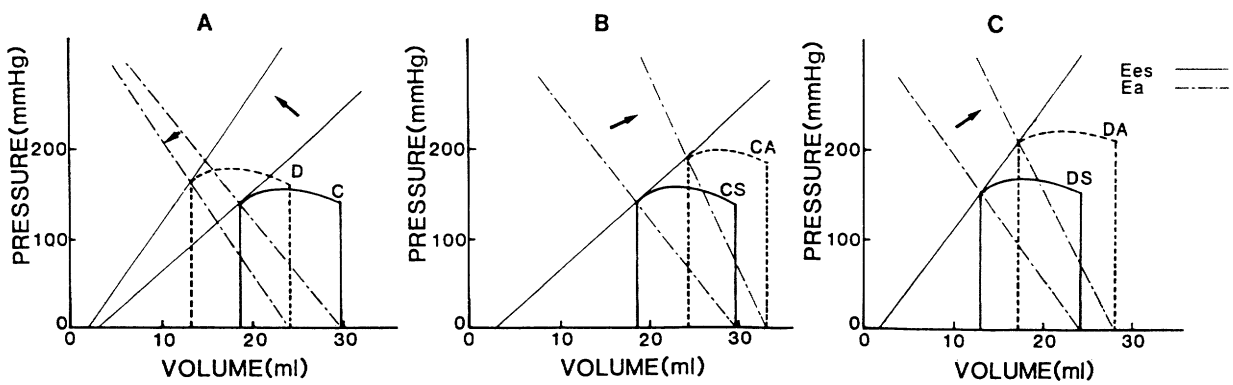

FIGURE 6. *A,* Effects of changes in contractility on the pressure-volume loop, Ees, and Ea during steady-state contractions. The solid pressure-volume loop (C) represents the control condition and the dashed loop (D) the dobutamine-enhanced contractile state. *B,* Effects of transient increases in afterload at control. The solid pressure-volume loop (CS) represents the steady state and the dashed pressure-volume loop (CA), increased afterload. *C,* Effects of transient increases in afterload during dobutamine-enhanced contractility. The solid pressure-volume loop (DS) represents the steady state and the dashed pressure-volume loop (DA), increased afterload. Arrows indicate the direction of changes in Ees and Ea.

energetically poor coupling between the left ventricle and the arterial system in that EW/PVA decreased with increases in afterload. This was probably because the transient increase in afterload was not sufficiently compensated for by rapid increases in preload, as indicated by the decrease in stroke volume (table 2).

In the control run stroke volume decreased because the increase in end-systolic volume induced by the increase in afterload was greater than that in end-diastolic volume (table 2), as shown in figure 6, *B*. Therefore, EW did not increase in proportion with the increase in end-systolic pressure and hence EW/PVA efficiency decreased in the control run. In contrast, during the dobutamine run, stroke volume did not decrease with increasing afterload (table 2), as shown in figure 6, *C*. Therefore, EW increased proportionally with the increase in end-systolic pressure and hence EW/PVA efficiency decreased much less than in the control run. In other words, a higher contractile state is associated with a greater reserve of EW after an abrupt increase in afterload.

Our study shows that an increase in left ventricular contractility increases both EW/PVA efficiency and EW for a given left ventricular end-diastolic volume during steady-state contractions. EW/VO_2 efficiency, or conventional mechanical efficiency, is the product of EW/PVA efficiency and PVA/VO_2 efficiency,[4–6] as shown in figure 1, *A*. Combined with the observation of simultaneous increases with the VO_2 component of nonmechanical activity and left ventricular contractility,[6, 27] finding of a dependency of EW/PVA efficiency on Ees and Ea facilitates understanding of the mechanisms of the wide variability in overall EW/VO_2 efficiency as a function of loading conditions and contractile state under physiologic and pathologic conditions. Direct study of EW/VO_2 and PVA/VO_2 efficiency was not the aim of this study.

Although we have not studied EW/PVA efficiency in a failing heart in this study, based on the theoretical prediction shown in figure 3, *B*, it is probably considerably decreased. Since the present method using the volumetric catheter can be applied clinically, EW/PVA efficiency and its dependence on Ees and Ea could be assessed by methods similar to those used here to obtain a better understanding of ventriculoarterial coupling in patients.

In summary, we evaluated not only Ees and Ea but also EW/PVA efficiency in the closed-chest dog with the use of a conductance catheter for measurement of ventricular volume, a catheter-tipped manometer in the left ventricle, and a Fogarty catheter placed in the thoracic descending aorta. The results show that an abrupt increase in afterload decreases EW/PVA efficiency and that enhancement of left ventricular contractility produces more efficient ventriculoarterial coupling and a greater reserve in the heart, in terms of EW/PVA efficiency, to meet an increase in afterload. We ascribe these changes in EW/PVA efficiency in the closed-chest dog to the relative changes in Ees and Ea in the pressure-volume diagram.

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