Left ventricular-arterial coupling relations in the normal human heart

This investigation was undertaken to assess left ventricular-arterial coupling relations in the normal human heart under varying loading conditions and inotropic states and thereby to establish whether the working point of the normal human heart is at optimal output or mechanical efficiency under basal hemodynamic conditions. In 22 patients with an atypical chest pain syndrome who had normal coronary arteriograms, left ventricular (LV) pressures, volumes, ejection fractions, and masses at cardiac catheterization, we acquired radionuclide angiograms in duplicate simultaneously with micromanometer LV pressures. These values were derived under control conditions and during methoxamine and nitroprusside infusions with heart rate held constant by right atrial pacing. Seven other patients underwent the same protocol but, in addition, we acquired these parameters during a steady-state, intravenous infusion of dobutamine (5 μg/kg/min). The interaction of LV chamber elastance (E_{es}) and effective arterial elastance (E_a) revealed that the normal human heart was operating at an E_{es}/E_a ratio of 1.62, a stroke work of 76 ± 31 gm-m, and a mechanical efficiency (stroke work to pressure-volume area ratio [SW/PVA]) of 0.65 ± 0.10. With an increase in LV load, the E_{es}/E_a ratio approached 1 ($p < 0.01$), LV stroke work increased ($p < 0.01$), and mechanical efficiency declined ($p < 0.01$). In contrast, during vasodilation, the E_{es}/E_a ratio increased to slightly above 2.0 ($p < 0.01$), LV stroke work decreased ($p < 0.001$), and mechanical efficiency improved ($p < 0.01$). During the dobutamine infusion, similar observations were made for E_{es}/E_a, LV stroke work, and SW/PVA over a similar range of LV loading conditions, but enhanced inotropy improved the energy transfer from the left ventricle to the arterial system at comparable E_{es}/E_a ratios without affecting mechanical efficiency. In conclusion, these data indicate that the normal human heart operates at neither optimal output nor efficiency. The working point, however, more closely approximates maximal mechanical efficiency than maximal LV output, but the normal human heart operates over a narrow range of LV SW values. (Am Heart J 1993;125:1659.)

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The performance of the left ventricle (LV) cannot be fully comprehended in the normal and diseased heart without understanding the interaction of the LV with the systemic arterial system. Sunagawa et al.[1, 2] have proposed a theoretic model to characterize this interaction. Using the end-systolic pressure-volume relation (E_{es}) to define LV chamber elastance and the end-systolic pressure (P_{es})–stroke volume relation to define effective arterial elastance (E_a), they proposed that the interaction of E_{es} and E_a would be useful for characterizing LV pump function under varying loading and inotropic conditions. Using an analytic model, Burkhoff and Sagawa[3] have shown that maximal LV stroke work occurs when the E_{es}/E_a ratio is near unity. The observation that maximal LV output or power occurs when the LV and systemic arterial system are optimally coupled has also been made by others.[2, 4-11]

Burkhoff and Sagawa[3] have also shown that maximal efficiency, defined as the ratio of LV stroke work to myocardial oxygen consumption, occurs when the ratio of E_{es} to E_a is near 2.0. They suggested that for normal physiologic LV pressures, end-diastolic volumes, stroke volumes, and ejection fractions to exist, the normal LV would probably operate closer to maximal efficiency rather than to maximal stroke work. Around what working point of LV output and mechanical efficiency the normal human heart is regulated under basal hemodynamic conditions has

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not been elucidated. Accordingly, this investigation was undertaken to assess the effects of alterations in LV load and inotropy on LV output and mechanical efficiency and thereby to determine whether the working point of the normal human heart is at optimal output or mechanical efficiency under basal hemodynamic conditions.

METHODS

Patient population. The study population consisted of 29 patients, who were referred for cardiac catheterization to evaluate an atypical chest pain syndrome. There were 23 men and 6 women, with an age range of 33 to 71 years (52 ± 10 [SD] years). All patients had a normal physical examination, electrocardiogram, chest radiograph, and normal coronary arteries at cardiac catheterization. The cardiac catheterization also demonstrated normal left ventricular pressures, volumes, ejection fractions, and masses. All patients had medications withheld for at least 24 hours. Each patient also provided written informed consent for the investigative protocol on forms approved by the Human Studies Committees at the University of Michigan or Veterans Administration Medical Centers, Ann Arbor, Mich.

Protocol. Following standard cardiac catheterization, 22 patients had radionuclide angiograms acquired in duplicate simultaneously with micromanometer LV pressures under control conditions and during methoxamine or nitroprusside infusions. Heart rate was held constant by right atrial pacing. Seven patients underwent this phase of the protocol and, in addition, they had radionuclide angiograms acquired in duplicate simultaneously with micromanometer LV pressures under control conditions and following methoxamine or nitroprusside infusions during the steady-state, intravenous administration of dobutamine (5 μg/kg/min).

Hemodynamics. The hemodynamic data acquisitions performed in this laboratory have been described in detail elsewhere.[12, 13] A bipolar right atrial pacing catheter was placed in the right atrial appendage to maintain heart rate constant, and a micromanometer catheter was positioned in the LV to measure LV and aortic pressures simultaneously with each radionuclide acquisition. These recordings were obtained for 10 to 20 cardiac cycles at the beginning, middle, and end of each radionuclide acquisition. An average LV pressure waveform was obtained and was hand-digitized.[14] The program developed in our laboratory yields instantaneous LV pressure and the first derivative of LV pressure at a variable sampling frequency from the peak of the R wave. It also allows for interpolation to provide LV pressure data points that correspond to the midpoint of each radionuclide frame.

Radionuclide angiography. The radionuclide angiographic data acquisitions performed in this laboratory have also been described in detail elsewhere.[15] Briefly, gated equilibrium radionuclide angiograms were acquired after in vivo red blood cell labeling with technetium-99m for 30 msec frames throughout the cardiac cycle for 250 cardiac cycles. During the midportion of each radionuclide acquisition, a 2 ml blood sample was drawn and was later counted for 2 minutes. This time delay was recorded for decay correction. At the end of the protocol, a distance measurement was obtained for attenuation correction. Attenuation-corrected radionuclide LV volumes were then calculated frame-by-frame from background-subtracted hand-drawn region-of-interest LV count data, decay-corrected blood sample counts, and attenuation correction, as previously validated in this laboratory.[16]

Data analysis. Corresponding micromanometer LV pressures and radionuclide LV volumes for each loading condition were plotted to obtain multiple pressure-volume loops for each patient. The maximal pressure/volume ratio from each pressure-volume loop was then subjected to linear regression analysis to obtain a slope (E_{es}) reflecting LV chamber elastance. Similarly, for each pressure-volume loop, P_{es}, defined as LV pressure at the maximum pressure/volume ratio, was divided by radionuclide LV stroke volume (SV), defined as the difference between the radionuclide maximum LV volume and radionuclide LV volume at P_{es}, to obtain a slope (E_a) reflecting effective arterial elastance.[1, 2] The coupling of the LV and systemic arterial system was then expressed as the ratio of E_{es}/E_a.

The pressure-volume area (PVA) as defined by Suga et al.[17, 18] was calculated for each LV loading condition and inotropic state. The PVA was defined as the area encompassed by E_{es}, the diastolic pressure-volume curve, and the systolic portion of each pressure-volume loop. LV stroke work (SW) was obtained by calibrated planimetry of each pressure-volume loop and then by multiplying by 0.0136 to convert from millimeters of mercury per milliliter to grammeters. LV pressure-volume areas are representative of the total mechanical energy available to the LV to perform external work. These areas have the components of external work and potential energy.[18] The latter can perform external work under the appropriate set of LV loading conditions.[19] It has also been shown that the LV PVA has a linear relationship with myocardial oxygen consumption.[20, 21] Therefore, since the traditional definition of myocardial efficiency is the ratio of external work performed to myocardial oxygen consumption (MVO_2), we used the LV SW/PVA relationship in this investigation to reflect the mechanical efficiency of converting the total mechanical energy (PVA) available to the LV to external work (SW). It is important to recognize that, although LV PVA has a linear relationship with MVO_2, there is a variable Y-axis offset caused by basal metabolism that is not reflected by PVA. Thus LV mechanical efficiency, as defined in this investigation, is not synonymous with myocardial efficiency.

It has previously been proposed that the position of the end-systolic pressure-volume relation may be quantitated in each heart by determining the volume (V) at a common P_{es}.[22] We quantitated the position of the end-systolic pressure-volume relation at a P_{es} of 125 mm Hg using the equation: $V_{125} = V_0 + 125/E_{es}$, where V_0 is the unstressed volume. This volume was chosen to approximate the average P_{es} value during control conditions and so that each E_{es} would be calculated from pressure/volume ratios that would encompass this value for P_{es}.

Further, we quantitated the effects of changes in LV

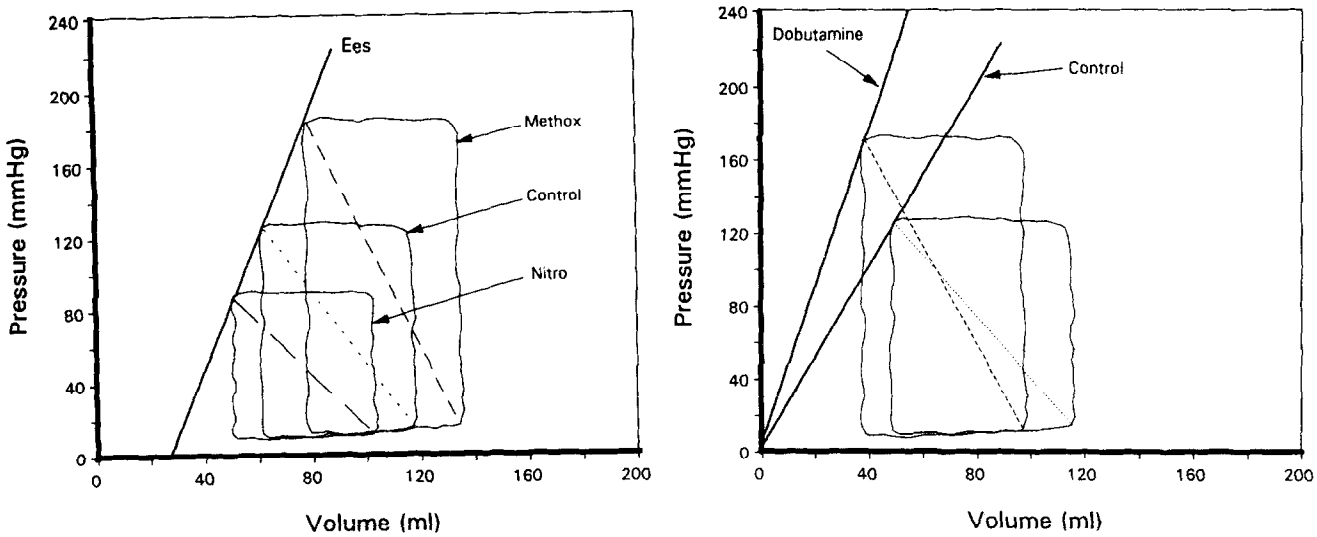

Fig. 1. Left panel, Schematic representation of the effects of altered LV load on effective arterial elastance and the relationship with LV chamber elastance. **Right panel,** Effects of enhanced inotropy on the relationship between LV chamber elastance and effective arterial elastance. E_{es}, LV chamber elastance; E_a, effective arterial elastance; *Methox*, methoxamine; *Nitro*, nitroprusside.

Table I. Effects of altered load on hemodynamics and left ventricular-arterial coupling

	E_{es} (mm Hg/ml)	V_o (ml)	P_{es} (mm Hg)	EDV (ml)	SV (ml)	E_a (mm Hg/ml)	E_{es}/E_a	SW_{100} (gm-m)	SW/PVA
Control	3.51 ± 1.26	1 ± 23	126 ± 18	99 ± 39	59 ± 20	2.32 ± 0.61	1.62 ± 0.80	76 ± 31	0.65 ± 0.10
Methoxamine			166 ± 23‡	112 ± 44*	62 ± 26	3.03 ± 1.21*	1.31 ± 0.68*	93 ± 42*	0.60 ± 0.11*
Nitroprusside			92 ± 16‡	86 ± 37†	57 ± 21	1.85 ± 0.70†	2.26 ± 1.51†	58 ± 25†	0.72 ± 0.13*

E_{es}, Left ventricular chamber elastance; V_o, unstressed volume; P_{es}, left ventricular pressure at end systole; E_a, effective vascular elastance; *EDV*, left ventricular end-diastolic volume; *SV*, left ventricular stroke volume; SW_{100}, left ventricular stroke work standardized to a common V_d of 100 ml; *SW/PVA*, left ventricular mechanical efficiency.
*$p < 0.01$, †$p < 0.001$, ‡$p < 0.0001$ versus control.

end-diastolic volume produced by variations in LV loading conditions and inotropic state on SW.[23, 24] This was done by establishing the LVSW at a common diastolic volume (V_d) of 100 ml. Finally, the LVSW at a V_d of 100 ml was then normalized to the maximal LVSW and was expressed as a percent of the maximal LVSW for comparison across the full range of E_{es}/E_a values.

Statistical analyses. The data are expressed as the mean ± 1 standard deviation (SD). To determine whether differences occurred between hemodynamic measures, E_a, E_{es}/E_a, SW_{100} (LV stroke work standardized to a common V_d of 100 ml), and SW/PVA at different LV loading conditions and inotropic states, an analysis of variance with repeat measures or paired *t* tests were performed. When a significant F statistic was obtained, multiple range tests were used to identify differences. Significant differences were established when a probability value of less than 0.05 was obtained.

RESULTS

Effects of LV load alterations on ventriculo-arterial coupling relations. The average LV E_{es} was 3.51 ± 1.26 mm Hg/ml. The values ranged between 1.65 and 5.61 mm Hg/ml. The average volume-axis intercept (V_o) for E_{es} was 1 ± 23 ml. The V_o values ranged from −23 to 81 ml. The effects of LV load alterations on hemodynamic parameters and left ventricular-arterial coupling relations are shown in Table I and are schematically demonstrated in Fig. 1. During control conditions, P_{es} averaged 126 ± 18 mm Hg, LV V_{ed} averaged 99 ± 39 ml, and LV stroke volume averaged 59 ± 20 ml. From these data, effective arterial elastance was calculated to be 2.32 ± 0.61 mm Hg/ml. Thus, the average effective arterial elastance was less than the average LV E_{es}, yielding an E_{es}/E_a ratio of 1.62 ± 0.80. The average LVSW was 76 ± 31 gm-m, and the conversion of total mechanical energy to external work (SW/PVA) averaged 0.65 ± 0.10.

Increasing LV load with methoxamine produced the expected effects on left ventricular-arterial coupling relations (Table I). The average P_{es} increased to 166 ± 23 mm Hg ($p < 0.0001$ vs control), as did LV

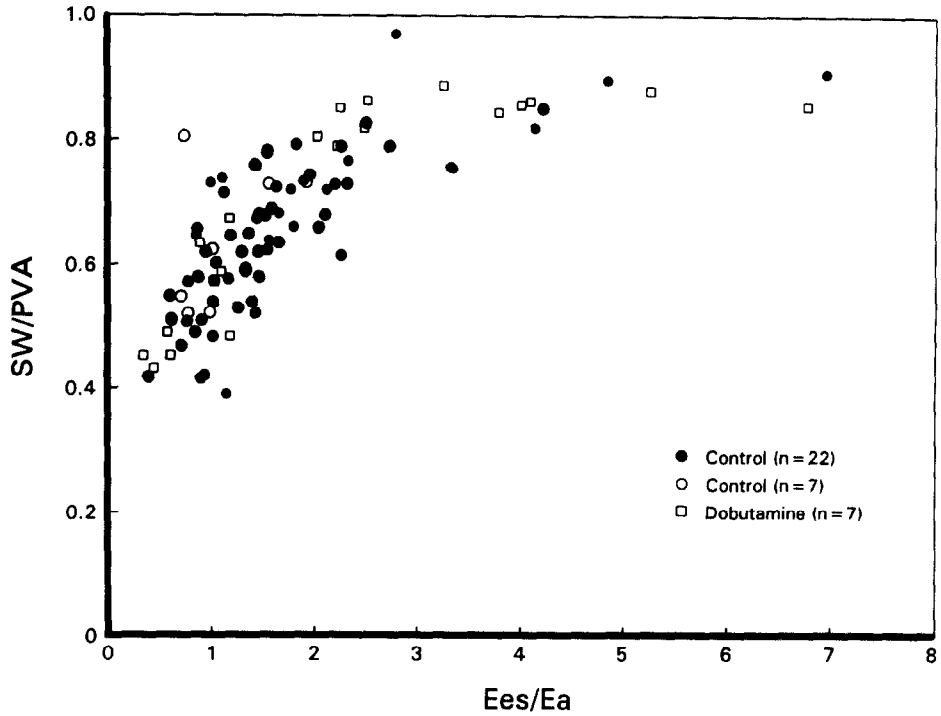

Fig. 2. Relationship between the efficiency of converting the pressure-volume area *(PVA)* to stroke work *(SW) (ordinate)* is compared with the left ventricular-arterial coupling relationship *(E_{es}/E_a) (abscissa).* From this relationship, the LV appears to operate over a wide range of left ventricular-arterial coupling ratios under basal conditions, while there is a sharp reduction in the efficiency of converting PVA to SW as the E_{es}/E_a ratio declines below 1.0, irrespective of inotropic state.

V_{ed} (112 ± 44 ml, $p < 0.01$), while LV stroke volume remained unchanged. Consequently, E_a increased to 3.03 ± 1.21 mm Hg/ml ($p < 0.01$). Nevertheless, E_a remained less than E_{es}, so that the LV-arterial coupling relationship continued to exceed 1.0 (1.31 ± 0.68, $p < 0.001$). During this loading condition, LVSW increased to 93 ± 42 gm-m ($p < 0.01$), but the mechanical efficiency of the LV was reduced to 0.60 ± 0.11 ($p < 0.01$).

Decreasing LV load with nitroprusside produced opposite effects on these hemodynamic parameters and on LV-arterial coupling relations (Table I). The average P_{es} was reduced (92 ± 16 mm Hg, $p < 0.0001$ vs control), as was LV V_{ed} (86 ± 37 ml, $p < 0.001$), while LV stroke volume was unchanged. E_a was therefore reduced to 1.85 ± 0.70 ($p < 0.001$). Consequently, the E_{es}/E_a ratio increased to 2.26 ± 1.51 ($p < 0.001$). With the reduction in LV load, LVSW decreased to 58 ± 25 gm-m ($p < 0.001$). However, the mechanical efficiency (SW/PVA ratio) of the LV improved to 0.72 ± 0.13 ($p < 0.01$).

A plot of the relationship between the efficiency of converting PVA to SW and E_{es}/E_a for all loading conditions in these 22 patients is shown in Fig. 2. As illustrated in the figure, the mechanical efficiency of the LV appears to reach a plateau at or just before an E_{es}/E_a value of 2.0. There is a sharp fall in the efficiency of converting PVA to SW as the E_{es}/E_a ratio declines, particularly to less than 1.0. This is illustrative of the detrimental effects of LV afterload on mechanical efficiency of the LV. In contrast, as E_{es}/E_a falls toward 1.0, LVSW increases, and as E_{es}/E_a increases, LVSW decreases. A plot of the relationship between normalized LVSW and E_{es}/E_a in Fig. 3 illustrates that, although normalized LVSW increases as the E_{es}/E_a ratio approaches 1.0, the LV operates over a narrow range of LVSW values. Thus, based on these observations, the LV operates under basal conditions over a broad range of E_{es}/E_a values within 9% of maximal mechanical efficiency, while normalized LVSW remains within 10% of maximal LVSW under basal hemodynamic conditions.

Effects of altered contractility on LV-arterial coupling relations. The effects of altered inotropy on hemodynamic parameters and LV-arterial coupling relations were also evaluated during a steady-state infusion of dobutamine in seven additional patients. These data are shown in Table II and are schematically demonstrated in Fig. 1. Dobutamine caused E_{es} to increase from 2.71 ± 1.07 to 4.93 ± 3.45 mm Hg/ml without a

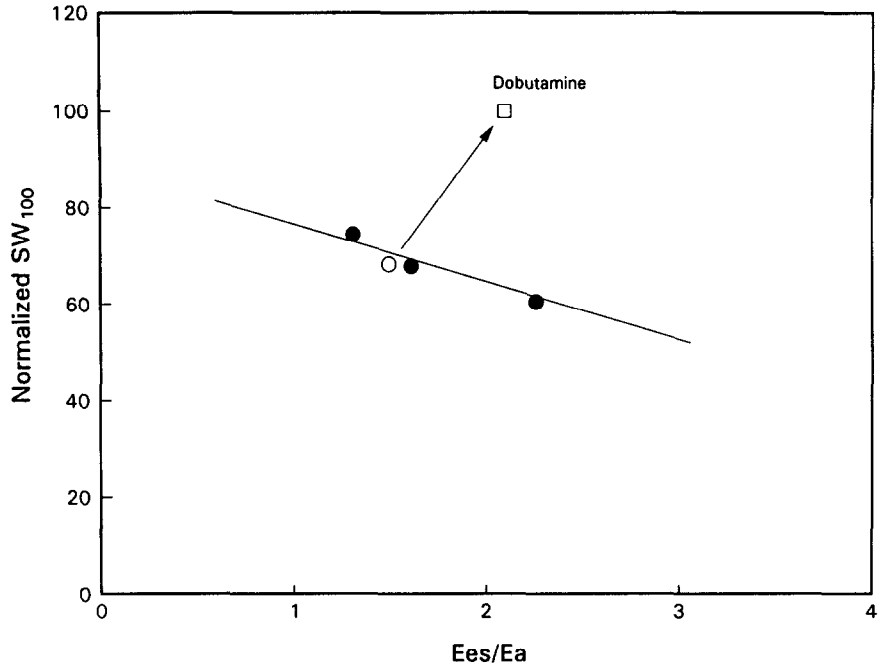

Fig. 3. LV stroke work *(SW)* values standardized to a LV diastolic volume of 100 ml have been normalized and plotted for each LV loading condition and inotropic state relative to the maximum LVSW *(ordinate)* and are compared with the E_{es}/E_a ratios *(abscissa)*. It is apparent that the normal LV operates over a broad range of LVSW values under basal contractile conditions, while enhancement of the inotropic state increases the energy transfer from the LV to the arterial system for any value of E_{es}/E_a.

Table II. Effects of altered inotropy on hemodynamics and left ventricular-arterial coupling

	E_{es} (mm Hg/ml)	V_o (ml)	P_{es} (mm Hg)	V_{125} (ml)	EDV (ml)	SV (ml)	E_a (mm Hg/ml)	E_{es}/E_a	SW_{100} (gm-m)	SW/PVA
Control	2.71 ± 1.07	−9 ± 14	127 ± 34	43 ± 16	114 ± 41	68 ± 26	2.02 ± 0.70	1.48 ± 0.66	78 ± 18	0.68 ± 0.11
Dobutamine	4.93 ± 3.45	−7 ± 17	158 ± 27*	28 ± 11†	97 ± 27	61 ± 22	2.92 ± 1.23*	2.06 ± 1.65	114 ± 27‡	0.69 ± 0.18

*$p \leq 0.05$, †$p < 0.01$, ‡$p < 0.001$ versus control.
V_{125}, Volume at a P_{es} of 125 mm Hg; other abbreviations as in Table I.

change in the volume-axis intercept (−9 ± 14 vs −7 ± 17 ml). This caused the V_{125} at a P_{es} of 125 mm Hg to decrease by 35% ($p < 0.01$). Dobutamine also caused an increase in P_{es} from 127 ± 34 to 158 ± 27 mm Hg ($p = 0.05$), while LV V_{ed} decreased insignificantly. E_a increased from 2.02 ± 0.70 to 2.92 ± 1.23 mm Hg/ml ($p < 0.05$), but this increase in E_a was not as great as the increase in E_{es}. Consequently, E_{es}/E_a also increased during the dobutamine infusion, from 1.48 ± 0.66 to 2.06 ± 1.65. Finally, LV stroke work standardized to a common V_d of 100 ml (SW_{100}) increased from 78 ± 18 to 114 ± 27 gm-m ($p < 0.001$), but the SW/PVA ratio was unchanged by dobutamine.

As shown in Fig. 2, the relationship between LV SW/PVA and E_{es}/E_a with dobutamine was similar to that under basal contractile conditions. In contrast, as shown in Fig. 3, the normalized LVSW is displaced upward for any comparable E_{es}/E_a ratio. Thus, a greater degree of energy transfer from the LV to the arterial system can be performed at a comparable mechanical efficiency during an enhanced inotropic state.

DISCUSSION

LV performance must be evaluated in the context of its interaction with the systemic arterial system. Recent investigations by Sunagawa et al.[1, 2] have demonstrated, in the isolated left heart preparation, that a theoretic model of the interaction between E_{es} and E_a can be used to evaluate LV systolic pump function. They showed that when E_{es} was matched with E_a, LVSW was optimized. A further theoretic investigation by Burkhoff and Sugawa[3] demonstrated

that over a range of contractile states, maximal LVSW occurred for each contractile state when E_a matched E_{es}. This fulfilled the original observation of Sunagawa et al.[1] They also demonstrated that myocardial efficiency, that is, the amount of external work performed for myocardial oxygen consumed, occurred during each contractile state when E_a was approximately one-half E_{es}. Moreover, myocardial efficiency demonstrated a stronger dependence on E_a than did LVSW during any stable contractile state. They, as did Sunagawa et al.,[1, 2] questioned whether it was possible to perform a physiologic amount of LV stroke volume at physiologic LV V_{ed} and P_{es} when E_a was equivalent to E_{es}. Both studies concluded that physiologic measures for these values would be more likely to occur when E_a was approximately one-half E_{es}.

The present investigation was undertaken to determine how the normal human heart operated under basal hemodynamic conditions. The important observation of this investigation was that, in the normal human heart, LV chamber elastance and effective arterial elastance are coupled to operate over a broad range at a working point that was at neither optimum, although it more closely approximated maximal mechanical efficiency than maximal LVSW. When E_a was increased using methoxamine, the E_{es}/E_a ratio approached 1.0. As a result, the LVSW increased compared with the control condition. In contrast, when E_a was reduced by nitroprusside, there was a modest increase in the E_{es}/E_a ratio at the expense of LVSW. However, when LVSW was normalized across the full range of LV loading conditions and the effects of preload on LVSW were considered, it was apparent that the normal human heart operated over a narrow range of LVSW values. At physiologic LV V_{ed} and P_{es}, LVSW was within 10% of maximal LVSW.

The data in this investigation are consistent with several experimental observations in various animal preparations. Several animal studies have shown that LVSW or power are maximal when the LV and arterial input impedances are matched. Wilcken et al.[4] have shown, in an open-chest canine preparation, that LVSW declines with changes in LV afterload. The observations made by Van den Horn et al.,[8] in an open-chest anesthetized cat preparation, also suggested that the LV operates to maximize LV output when physiologically loaded. This observation was carried further by Myhre et al.[9] in an open-chest canine preparation, which showed that SW was matched to LV load. However, injection of microspheres into the left coronary circulation to produce LV dysfunction demonstrated that external output was less than maximum, suggesting an afterload mismatch when the LV was failing. Moreover, Elzinga et al.,[25] studying feline hearts on a Langendorf apparatus, showed that both the right and left ventricles were matched to the input impedances of their respective arterial systems, since both ventricles produced maximum power under normal physiologic loading conditions. In a closed-chest, conscious dog preparation, Little and Cheng[11] demonstrated that LVSW was maximum when the E_{es}/E_a ratio was nearly 1.0.

Our data in the normal human heart also demonstrate that as the E_{es}/E_a ratio approaches 1.0, LVSW increases toward a maximum. This was achieved at normal LV end-diastolic volumes and stroke volumes, but it required a P_{es} value of 166 mm Hg, which was clearly in excess of what would be considered physiologic under basal hemodynamic conditions. Therefore, it would seem unlikely that the normal human heart operates to maximize LVSW under normal operating conditions. An E_{es}/E_a ratio of 1.0 would be achieved only at nonphysiologic levels of LV load or possibly with LV dysfunction, which was not tested in this study. Nevertheless, these data also demonstrate that the normal human heart operates over a narrow range of LVSW values under basal hemodynamic conditions, suggesting a relative insensitivity of LVSW to LV load during basal contractile conditions.

Other studies have demonstrated that maximum LVSW or power do not coincide with optimal myocardial efficiency. Elzinga and Westerhof[26] demonstrated, in an isolated physiologically ejecting feline heart preparation, that LV power was maximized at higher afterload resistance than that which optimized myocardial efficiency. Piene and Sund[7] demonstrated that right ventricular pump function efficiency was maximal when pulmonary impedance and ejection from the right ventricle were in the physiologic range. Myhre et al.[10] have also shown, in open-chest anesthetized dogs, that the working point of the LV may not necessarily coincide with optimal LV external work. They suggested that under control conditions the LV and arterial load may not be optimally coupled, but the offset that they observed was too small to indicate whether the LV was controlled to maximize external work or efficiency. Finally, Burkhoff and Sagawa[3] have shown that the optimal coupling between the LV and the systemic arterial system needed to maximize LVSW occurs when the LV and arterial elastance values are matched, while maximal efficiency occurs when E_a is approximately one-half E_{es}.

The average E_{es}/E_a value of 1.62 under basal hemodynamic conditions in our patients was similar

to that observed in a preliminary report by Jones et al.[27] In nine isolated canine LV preparations, they reported that this E_{es}/E_a ratio corresponded to maximal myocardial efficiency. When they normalized the myocardial efficiency values to a maximal myocardial efficiency value of 1.0, a wide range of E_{es}/E_a values around a normalized myocardial efficiency of 1.0 occurred, suggesting that the LV operates within 20% of this peak value. Recently, Asanoi et al.[28] calculated E_{es} and E_a in 12 normal patients using micromanometer LV pressures and M-mode echocardiograms. Interestingly, they noted that the E_{es}/E_a ratio in these patients was approximately 2.0. In the present investigation, it is important to note that a broad range of E_{es}/E_a values exists at or near maximal mechanical efficiency. These data tend to confirm previous suggestions[3] that for physiologic values of P_{es}, LV V_{ed}, and LV stroke volume to occur, the E_{es}/E_a ratio must reside somewhere above 1.0. Moreover, the relative sensitivity of LV mechanical efficiency to changes in loading conditions, in contrast to LV output, also suggests that the working point of the normal human heart may be regulated more by mechanical or myocardial efficiency than by maximal output or power.

The data in this investigation also demonstrate that LV mechanical efficiency is not reduced by an increase in LV contractility, despite enhanced energy transfer from the LV to the arterial system in the form of augmented normalized LVSW. This observation is consistent with the findings of previous clinical studies.[29-31] These data suggest that the LV moves to a higher relationship between SW and E_{es}/E_a, so that mechanical efficiency may be less sensitive to alterations in LV loading conditions.

Potential limitations to this investigation are based on the assumptions that were used. We did not estimate MVO_2 and therefore we could not calculate myocardial efficiency. We assumed, however, a linear relationship between MVO_2 and PVA.[20, 21] Despite this linear relationship, there is a Y-axis offset to the MVO_2/PVA relationship, which reflects a basal energy requirement, and therefore mechanical efficiency (SW/PVA) cannot be equated to myocardial efficiency (SW/MVO_2). The average E_{es}/E_a value of 1.62 under basal hemodynamic conditions in our patients and in the preliminary reports by Jones et al.[27] lends support to the hypothesis that the normal human heart may have an operating point closer to maximal mechanical efficiency or myocardial efficiency under basal hemodynamic conditions then to maximal output. However, to prove this hypothesis, further investigations in patients with normal human hearts will be required.

We also assumed that E_{es} was linear. However, E_{es} may not be linear over the full range of LV loading conditions.[32-34] This may be particularly true at the extremes of LV load. It has been shown that a reduction in LV pressure and thus in coronary perfusion may cause this relationship to become curvilinear toward the volume axis.[34] The observation that only a fraction of the potential energy stored within the LV at end systole can be converted to external work under an appropriate set of loading conditions because of shortening deactivation or cross-bridge interference at short sarcomere lengths, further suggests a curvilinear relationship.[19] In addition, we assumed that E_{es} was not affected by steady-state alterations in LV loading conditions. It has been previously shown that changes in LV loading conditions may cause a shift in the E_{es} relationship.[35]

The final assumption of this investigation was the description of arterial load in terms of E_a. Recent preliminary information would suggest that utilization of E_a to characterize arterial load is not unreasonable in the normal heart, since E_a appears to reflect the major components of vascular load under normal conditions.[36, 37] It has been suggested that E_a ignores the higher frequency components of arterial impedance because it assumes constancy of arterial pressure. The data of Latham et al.[36] in the nonhuman primate and of Kelly et al.[37] in hypertensive patients suggest that the use of E_a to approximate total vascular load is appropriate. Thus, in the normal human heart, E_a is probably a reasonable characterization of total vascular load, and it may be useful for characterizing total vascular load in patients with cardiac pathology to improve our understanding of LV and arterial interactions.

In conclusion, the data from this investigation suggest that under basal LV loading conditions, the interaction of the normal human heart with the systemic arterial system operates over a broad range, and the working point of the normal human heart is not at either optimum, neither maximal mechanical efficiency nor maximal LV output. The utility of this concept for clarifying the effects of pathologic conditions on the LV-arterial coupling relation remains to be defined.

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