Optimal Arterial Resistance for the Maximal Stroke Work Studied in Isolated Canine Left Ventricle

Kenji Sunagawa, W. Lowell Maughan, and Kiichi Sagawa

SUMMARY. In a previous analysis of ventricular arterial interaction (Sunagawa et al., 1983), we represented the left ventricle as an elastic chamber which periodically increases its volume elastance to a value equal to the slope of the linear end-systolic pressure-volume relationship. Similarly, the arterial load property was represented by an effective elastance which is the slope of the arterial end-systolic pressure-stroke volume relationship. Since the maximal transfer of potential energy from one elastic chamber to another occurs when they have equal elastance, we hypothesized that the left ventricle would do maximal external work if the ventricular elastance and the effective arterial elastance were equal. We tested this hypothesis in 10 isolated canine left ventricles, ejecting into a simulated arterial impedance, by extensively altering arterial resistance and finding the optimal resistance that maximized left ventricular stroke work under various combinations of end-diastolic volume, contractility, heart rate, and arterial compliance. Each of these parameters was set at one of three levels while others were at control. The optimal resistance varied only slightly with arterial compliance, whereas it varied widely with contractility and heart rate. We thus determined that the ratio of the optimal effective arterial elastance to the given ventricular elastance remained nearly unity. This result supports the hypothesis that the left ventricle does maximal external work to the arterial load when the ventricular and arterial elastances are equalized.

(Circ Res 56: 586-595, 1985)

THE purpose of the cardiovascular system is to provide adequate blood flow to peripheral tissues and thus support the normal function of these tissues. Whereas adequate cardiac output for peripheral perfusion can be achieved by multiple combinations of ventricular contractility and loading conditions, it is likely that the cardiovascular control system uses a unique combination of ventricular contractility, heart rate, and arterial impedance characteristics which optimizes ventricular performance from an energetics point of view. This question of optimum coupling can be answered by studying the energy-related ventricular variables that generate adequate cardiac output, to determine whether some are maximized (or optimized in some other way) at a certain combination of arterial impedance and ventricular contraction characteristics. The list of energy-related ventricular variables includes stroke work, mean or peak stroke power, and the myocardial oxygen cost of these variables.

The mean stroke power output of the normal excised feline left or right ventricle was found to be maximum when the ventricle was loaded with normal arterial impedance (Elzinga et al., 1980). Also, in the cat right ventricle, pump efficiency (defined as the ratio of external stroke work to total theoretically usable energy) was found to be maximum at normal pulmonary arterial impedance (Piene and Sund, 1982). However, it is not known how multiple combinations of changes in end-diastolic volume, ventricular contractility, heart rate, and arterial resistance and compliance, which probably vary under physiological conditions, affect ventricular performance and energetic variables.

In a recent analysis (Sunagawa et al., 1983), we predicted that maximal stroke work results when the end-systolic elastances of the ventricle and arterial load are equal. The purpose of this study was to test this prediction. We decided that external stroke work was the coupling variable to be optimized, because perfusion of vital organs (such as brain, heart, and kidney) requires both adequate stroke volume and adequate arterial pressure, which can be integratively accounted for by the stroke work. In order to cover a wide range of physiological coupling conditions between the ventricle and the arterial system, we varied left ventricular end-diastolic volume, ventricular contractility, heart rate, or arterial compliance independently, at three levels, and combined each of these changes with changes in arterial resistance at multiple levels. By analyzing the stroke work data determined under these conditions, we did arrive, as predicted, at a simple unifying notion of the optimal ventriculoarterial coupling in terms of the relative magnitude of ventricular end-systolic elastance and arterial effective volume elastance.

Because the present analysis with an isolated heart preparation deals only with the fundamental mechanics of ventriculoarterial coupling, our criterion for design optimization may not necessarily be valid for a normally functioning animal which responds
to various environmental stimuli. In such a circumstance, the criterion for optimizing circulatory system control probably is multi-factorial, and undoubtedly varies dynamically with the nature of given stimuli. The validity also may not hold for pathological circumstances, where physiological principles are likely to be compromised or distorted.

Methods

Preparation

The surgical preparation of an isolated canine ventricle has been described elsewhere (Suga and Sagawa, 1977; Sunagawa et al., 1982a). Briefly, in each experiment we used a pair of mongrel dogs (20–22 kg), anesthetized with sodium pentobarbital (30 mg/kg, iv). The chest of the heart donor was opened under artificial ventilation, and the subclavian artery and right atrium were cannulated and connected to the femoral arteries and veins, respectively, of a support dog. Post mortem, the azygous vein, thoracic duct, left and right venae cavae, brachiocephalic artery, descending aorta, and pulmonary hilum, the heart was removed from the chest. The pericardium was removed, the left and right ventricles were vented, and the chordae tendinae were cut. A thin balloon mounted on a plastic adaptor was placed in the left ventricle and the adapter was sewn into the mitral valve annulus. The balloon adaptor then was connected to a ventricular volume control servo-pump system (Suga and Sagawa, 1977; Sunagawa et al., 1982b). A constant volume of tap water filled the pump and balloon. Therefore, absolute volume changes in the balloon were precisely controlled and measured by the volume servo-pump. A disc oxygenator (Pemco model 7109) was placed in parallel with the support dog so that oxygenated blood could be received either from the support dog or from the oxygenator, as desired. Coronary arterial pressure was measured by a catheter placed via the brachiocephalic trunk in the aortic root. A servo-controlled perfusion pump (Harvard Apparatus model 1215) maintained mean coronary arterial pressure at 100 mm Hg throughout the experiment. Coronary arterial blood temperature was maintained at approximately 37°C with a heat exchanger. The left ventricular pressure was measured in the balloon with a catheter tip micromanometer (Millar model PC-380). Ventricular pressure-volume loops were monitored on-line on an X-Y tip micromanometer (Millar model PC-380). Ventricular pressure was integrated with respect to volume. To calculate external stroke work on-line digitally, instantaneous ventricular pressure measured in the isolated heart preparation were recorded simultaneously with arterial pressure of the support dog, on the same chart recorder.

Impedance-Loading System

We used a modified version of the impedance loading system for the isolated canine ventricle previously reported by Sunagawa et al. (1982c). Basic characteristics and performance are essentially the same as those of the previous one. Briefly, we simulated the arterial afterload system with a 3-element (Westerhof et al., 1971) Windkessel model, and the preload system with a simple dc pressure source coupled with a filling resistance in series (Fig. 1). In the original impedance-loading system, we digitally calculated the instantaneous flow every 2 msec with a high-performance 16-bit microprocessor (Intel 8086/8087) by feeding digitized instantaneous ventricular pressure to pre- and afterloading system models. The calculated instantaneous flow as then numerically integrated with respect to time, and the integral was used as the command signal to the volume servo-pump through a 12-bit digital to analog converter. Compared with the analog computer-based system, arterial impedance generated by this system is much more precise and reliable. With the loading system, the ejection pattern and stroke volume of a given left ventricle depended on its interaction with the afterload system parameters (R, R, and C) set in the arterial model. To calculate external stroke work on-line digitally, ventricular pressure was integrated with respect to volume over each cardiac cycle and recorded on a chart recorder as an analog signal. Ventricular pressure and volume and aortic pressure of the isolated heart preparation were recorded simultaneously with arterial pressure of the support dog, on the same chart recorder.

Protocols

Protocol 1: Effect of End-Diastolic Volume on Optimal Arterial Resistance

In eight ventricles, we changed end-diastolic volume at three different levels (i.e., 35, 30, and 25 ml) under a constant inotropic background. At each end-diastolic volume, we obtained multiple pressure-volume loops as shown in panel A of Figure 2 by successively decreasing arterial resistance (R in panel B of Fig. 1) to 79.4% of the preceding test R value. The initial R value was always set at 8.0 mm Hg/ml sec. Repeating the constant fractional reduction in arterial resistance 11 times yielded the smallest resistance of 0.8 mm Hg/sec ml, which is one-tenth of the starting value. With this 10-fold reduction in arterial resistance, the ventricle changed stroke volume over a wide range. At each resistance value, we waited for the ventricle to reach a steady state, and only the steady state during the subsequent 10 seconds was used for analysis. Panel B of Figure 2 shows a typical strip chart recording from one entire sequence. Heart rate was maintained at 120 beats/min by right atrial pacing. Arterial compliance and characteristic impedance were fixed at their control values, 0.4 ml/mm Hg and 0.2 mm Hg/ml sec, respectively (Sunagawa et al., 1982c).

Protocol 2: Effect of Changes in Contractility on the Optimal Arterial Resistance

We measured ventricular contractility from the slope (Em) of the end-systolic pressure-volume relationship, which was determined by applying linear regression analysis on the left upper corners of the pressure-volume loops, as shown in Figure 2A. In seven ventricles, we changed contractility of the left ventricle at three levels by

![Diagram](https://via.placeholder.com/150)

**FIGURE 1.** An electrical analogue of the 3-element Windkessel arterial model (Westerhof et al., 1971). R, = characteristic impedance; C, = arterial compliance; R, = arterial resistance.
Intracoronary infusion of dobutamine, starting at 10 \( \mu \)g/min and titrating to a 20% increase in \( E_{\text{sw}} \). At each level of contractility, we obtained multiple pressure-volume loops by reducing arterial resistance stepwise, as described in protocol 1, while maintaining end-diastolic volume constant at 35 ml. Heart rate, arterial compliance, and characteristic impedance were also fixed at their control values throughout this protocol. When dobutamine increased heart rate above the paced rate (120 beats/min), the pacing rate was increased so that the chronotropic intervention would not occur.

Protocol 3: Effect of Changes in Heart Rate on the Optimal Arterial Resistance

Seven ventricles were paced at three different heart rates: 120, 140, and 160 beats/min. At each heart rate, we obtained multiple pressure-volume loops by reducing arterial resistance stepwise, as described in protocol 1. End-diastolic volume was fixed at 35 ml. Arterial compliance and characteristic impedance were maintained constant at their control values throughout this protocol.

Protocol 4: Effect of Changes in Arterial Compliance on the Optimal Arterial Resistance

In seven ventricles, we set the arterial compliance to three different values, 0.2, 0.4, and 0.8 ml/mm Hg, under a constant inotropic background. At each compliance value, we obtained multiple pressure-volume loops by reducing arterial resistance stepwise, as described in protocol 1, while maintaining characteristic impedance and heart rate constant at their control values. End-diastolic volume was fixed at 35 ml.

Data Analysis

To test the significance of effects of changes in end-diastolic volume, contractility, heart rate, and arterial compliance on the magnitude of external stroke work and the optimal arterial resistance, we used repeated-measure
Table 1
Effects of End-Diastolic Volume, Contractility, Heart Rate, and Arterial Compliance on the Slope ($E_a$) and Volume Axis Intercept ($V_o$) of Ventricular End-Systolic Pressure-Volume Relationship

<table>
<thead>
<tr>
<th>End-diastolic volume (ml)</th>
<th>Contractility</th>
<th>Heart rate (beats/min)</th>
<th>Arterial compliance (ml/mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>Low</td>
<td>120</td>
<td>0.2</td>
</tr>
<tr>
<td>30</td>
<td>Med</td>
<td>140</td>
<td>0.4</td>
</tr>
<tr>
<td>35</td>
<td>High</td>
<td>160</td>
<td>0.8</td>
</tr>
<tr>
<td>$E_a$ (mm Hg/ml)</td>
<td>5.6±1.3</td>
<td>5.4±1.2</td>
<td>5.2±0.7</td>
</tr>
<tr>
<td></td>
<td>4.1±1.1*</td>
<td>5.8±1.9*</td>
<td>7.5±2.3*</td>
</tr>
<tr>
<td></td>
<td>4.5±0.9</td>
<td>4.9±0.8</td>
<td>4.6±0.4</td>
</tr>
<tr>
<td>$V_o$ (ml)</td>
<td>7.3±2.3</td>
<td>7.0±2.2</td>
<td>6.2±2.8</td>
</tr>
<tr>
<td></td>
<td>5.4±3.5</td>
<td>4.3±2.6</td>
<td>3.2±2.9</td>
</tr>
<tr>
<td></td>
<td>5.4±2.7</td>
<td>4.9±2.5</td>
<td>5.4±3.5</td>
</tr>
<tr>
<td></td>
<td>5.4±3.7</td>
<td>4.7±3.7</td>
<td>4.4±3.3</td>
</tr>
</tbody>
</table>

Data are presented in mean ± SEM values.

*P < 0.001.

Results
Table 1 summarizes the slope ($E_a$) and volume axis intercept ($V_o$) of the end-systolic pressure-volume relationship under these four protocols. $E_a$ was altered only when contractility was changed. Figure 3 summarizes the effects of end-diastolic volume (panel A), contractility (panel B), heart rate (panel C), and arterial compliance (panel D) on the external stroke work vs. arterial resistance relationship. In all experimental conditions, the stroke work was 50–69% of the maximal value with the initial, largest arterial resistance of 8 mm Hg/sec per ml. The stroke work increased rapidly with the decrease in arterial resistance. There was always one optimal arterial resistance at which the stroke work peaked. When arterial resistance was further decreased toward 0.8 mm Hg/sec per ml, the stroke work decreased.

Figure 3. Effects of changes in arterial resistance on the stroke work under various end-diastolic volumes (panel A), contractilities (panel B), heart rates (panel C), and compliances (panel D). Stroke work is calculated on-line as the developed pressure-volume area per cardiac cycle. Stroke work reached its peak value as the arterial resistance decreased from 8 to a certain value. Further reductions of arterial resistance decreased stroke work.
mm Hg/sec per ml, the stroke work started decreasing again, although it did not decrease to the same level obtained with the largest resistance (panel B, Fig. 2). By increasing end-diastolic volume, the stroke work could be increased at any given arterial resistance (panel A, Fig. 3). Optimal resistance did not change significantly. Increases in contractility increased the stroke work by any given arterial resistance (panel B). Unlike the effect of changes in end-diastolic volume, however, the optimal arterial resistance became larger with increases in contractility (panel B). As shown in panels C and D of Figure 3, there was no consistent relationships between heart rate and the optimal arterial resistance or between arterial compliance and the optimal arterial resistance.

Influences of changes in end-diastolic volume, contractility, heart rate, and arterial compliance, specifically, on the maximal external stroke work and optimal arterial resistance are summarized in Figure 4. Maximal stroke work increased significantly \((P < 0.0001)\) with increases in end-diastolic volume. However, optimal arterial resistance did not change significantly. Increases in contractility altered the maximal stroke work \((P < 0.0001)\) with concomitant increases in the optimal arterial resistance \((P < 0.0001)\). Alterations in heart rate did not change the maximal stroke work. The optimal arterial resistance tended to decrease with increases in heart rate, although this trend was not statistically significant (panel C). Increases in arterial compliance did slightly increase \((P < 0.01)\) the maximal stroke work (panel D). Although quantitatively small, the optimal resistance significantly increased \((P < 0.01)\) with increases in arterial compliance (panel D).

**Discussion**

We have shown that increases in end-diastolic volume increased the maximal stroke work without changing the optimal arterial resistance, whereas increases in contractility, which increased the maximal stroke work, did increase the optimal arterial resistance. The optimal arterial resistance tended to decrease with increases in heart rate, although it was statistically insignificant. In order to clarify the general rule that determines the optimal arterial resistance, we have used the framework of analysis that was previously proposed for prediction of stroke volume under variable ventriculoarterial coupling conditions (Sunagawa et al., 1983).

**Analysis of Optimal Loading by a Framework of Ventriculoarterial Coupling**

The end-systolic pressure-volume relationship is approximately linear over a physiological range, and is relatively insensitive to changes in loading conditions (Suga et al., 1973, 1979; Suga and Sagawa, 1974). This relationship is illustrated in the left panels of Figure 5. The mechanical characteristics of the arterial system can be represented by the relationship of arterial end-systolic pressure to stroke volume \((P_{es}-SV relationship)\) as shown in the third right panel of Figure 5. The larger the stroke volume ejected into the arterial system, the greater the generated \(P_{es}\) will be. In the fourth, righthand panel of Figure 5, the volume axis is simply reversed, so that the stroke volume is plotted with zero reference to some specified end-diastolic volume for the left ventricle. The equilibrium SV when the ventricle is coupled with the arterial system can be obtained from the intersection between these two \(P_{es}-LVV\) relationship lines (bottom panel). Although this coupling framework is extremely simple, stroke volumes predicted by this method were indeed very close to experimentally determined stroke volumes (Sunagawa et al., 1983).

In this coupling framework, the arterial system was treated as if it were an elastic chamber with a
Figure 5. A schematic illustration of the framework of analysis for coupling the ventricle with the arterial load. The mechanical characteristics of the left ventricle are expressed by the end-systolic pressure ($P_{es}$) vs. volume ($LVV$) relationship (left middle panel). The mechanical characteristics of the arterial system is expressed by the arterial end-systolic pressure ($P_{es}$) vs. stroke volume ($SV$) relationship (right middle panel) which can be transformed into the $P_{es}-LVV$ relationship. The equilibrium end-systolic pressure and volume when the ventricle is coupled with the arterial system are obtained from the intersection between these two $P_{es}-LVV$ relationship lines (bottom panel).

Volume elastance $E_a$ (Appendix 1), just as we treated the ventricle as an elastic chamber with an end-systolic volume elastance $E_{es}$. With such representations, one can predict analytically (see Appendix 2) or intuitively, from the diagram in Figure 6, that mechanical energy transferred from the ventricular elastance to the arterial elastance will become maximal when the slopes of the ventricular and arterial $P_{es}-SV$ relationships, $E_{es}$ and $E_a$, are equal to one another. Under this optimally loaded condition, an effective ejection fraction defined as the ratio of stroke volume to the effective end-diastolic volume would be 50%. To test these predictions, we directly determined the optimal slope $E_a$ of the arterial $P_{es}-SV$ relationship in each of four different protocols by calculating the ratio of the arterial end-systolic pressure to the stroke volume when the arterial resistance was optimal. The $P_{es}$ was measured as the arterial pressure at the end of ejection. As shown in the bottom panel of Figure 7, the ratio of the optimal $E_a$ thus calculated to the $E_{es}$ of a given ventricle was quite close to unity, despite a wide variety of end-diastolic volumes, contractilities, heart rates, and arterial compliances. The effective ejection fraction in all the optimized conditions was also found to be nearly 50%, as shown in the top panel of Figure 7. Therefore, our hypothesis that the arterial elastance will be equal to ventricular elastance when the external stroke is maximal was shown to be valid.

Figure 8 further clarifies our points by plotting the experimentally determined average relationships between end-systolic pressure and stroke volume of both the ventricle and the arterial system in each protocol. Changes in end-diastolic volume did not change the ventricular end-systolic pressure-volume relationship (panel A). Therefore, there were no substantial differences in arterial elastance which
maximized the stroke work. Changes in contractility changed the ventricular elastance. The maximal stroke work resulted when the arterial volume elastance was increased in parallel with the increases in ventricular volume elastance (panel B of Fig. 8). Changes in heart rate or compliance in the range presently studied did not significantly affect the ventricular end-systolic pressure-volume relationship. Therefore, the arterial elastance that maximized stroke work also remained unaltered (panels C and D of Fig. 8).

Influences of changes in preload, arterial compliance, contractility, and heart rate on the optimal arterial resistance, rather than elastance, can also be predicted quantitatively with this framework of analysis. If we approximate the end-systolic pressure by mean arterial pressure, the effective arterial elastance \( E_a \) can be approximated by the ratio of total resistance to cardiac cycle length (Appendix 1). With this approximation, the total resistance that maximizes stroke work is determined simply as the product of \( E_a \) and cardiac cycle length \( T \) (Eq. 9 in Appendix 3). Because this simplified formula \( (R_{T,\text{opt}} = E_a \cdot T) \) for optimal resistance contains neither preload nor physical compliance of the arterial system, it suggests that changes in end-diastolic volume or arterial compliance would not affect the optimal resistance at all. If, on the other hand, the ventricular contractility increases, a larger arterial resistance is required for the optimal condition. All these predictions were found to be consistent with the experimental data. The optimal resistance formula also leads to a prediction that a mere increase in heart rate, which slightly shortens \( T \) without a change in \( E_a \), would slightly decrease the optimal arterial resistance. This prediction was also substantiated, although the decrease in optimal resistance was not statistically significant. Had we extended the heart rate change to a much lower range, (e.g., between 120 and 60 beats/min), we might have seen significant changes in the optimal arterial resistance.

Only a few studies in the literature have addressed...
the effect of changing arterial compliance alone on stroke work output of the left ventricle. Elzinga and Westerhof (1973) coupled a hydraulic model of arterial impedance with isolated cat hearts and determined the effect of multiple combinations of arterial resistance and compliance on left ventricular pressure and outflow and aortic pressure. From these data, Noble (1979) calculated the relationship of mean power output (stroke work times heart rate per minute) to mean aortic pressure under two different arterial compliance values (Fig. 4.6 of the cited reference). When the compliance value was set at 8% of the normal, the maximum stroke work was reduced to less than one-half of control. This drastic effect of compliance may appear to be contradictory to the very small effect observed in our study. In fact, the seemingly large difference comes from the extremely large reduction of arterial compliance down to 8% of normal, used in Elzinga and Westerhof’s experiment, as opposed to the more physiological magnitude of compliance changes (to 50% and 200% of normal) in the present experiment. The data from the same cat heart suggest (although not enough information was provided) that when the compliance was decreased to 37% of control, the stroke work did not fall by more than 10%. Therefore, those authors demonstrated that a large reduction in arterial compliance can markedly reduce flow and work output from the left ventricle, whereas we showed that more physiological magnitudes of arterial compliance change do not cause such a drastic effect.

**Nature’s Design for Ventrículoarterial Matching**

The analysis described in the previous section validated the prediction from our previous study that ventricular stroke work will be maximized when the ventricular and arterial elastances are matched in magnitude (Sunagawa et al., 1983). Whether the maximum external stroke work is really the crucial criterion that an organism uses for optimizing the operation of the cardiovascular system in physiological circumstances is an entirely different question, and one which remains to be answered.

It is well known that the physiological value of the ejection fraction in many animal species, including man, is approximately 50% or slightly larger. Considering the fact that $V_o$ is negligibly small relative to the end-diastolic volume in vivo, the average ejection fraction of 47% observed in anesthetized dogs (Tsakiris et al., 1969) may be regarded as supportive evidence for the theory that maximal external work may be the optimization criterion in intact animals as well.

It is notable, however, that the decrease in the external work with mild deviations of arterial resistance from the optimum value is rather slight, as evidenced by the flatness of the work curves around the maximum region (Fig. 3). Over the same range of arterial resistance, the ventricular ejection fraction can change much more significantly. Therefore, the 50% ejection fraction observed under the optimal matching could occur for a totally different reason, and does not prove that the maximal external work is used as the optimization criterion.

Any hypothesis concerning physiological matching of cardiac performance with arterial load must eventually be tested and validated in an intact animal under various physiological conditions. Needless to say, our study with isolated hearts does not mimic the in vivo situation. Nevertheless, the information from the present study attests to the compatibility of our hypothesis with the basic mechanical property of the ventricular pump. We believe that the hypothesis will be useful in interpreting other data from intact animals.

**Limitations**

In this investigation, we maintained coronary arterial pressure constant throughout the experiments, regardless of the ventricular loading conditions. In the real ventriculoarterial coupled system, coronary arterial pressure is determined as the result of hydraulic interactions of the ventricle with the arterial impedance. Because coronary arterial pressure can modulate the ESPVR if it falls below a critical level (Sunagawa et al., 1982a), the optimal matching will be determined in a somewhat more complex manner than analyzed here. Therefore, the proposed framework is valid only when the ventricle is operating, as it normally does, in a range of arterial pressures over which the ESPVR is insensitive to changes in coronary perfusion pressure.

In this analysis, we used the 3-element Windkessel model (Westerhof et al., 1971) to approximate arterial input impedance. Although this arterial model does not reproduce the fluctuations of impedance modulus over the high frequency range, due to wave reflections, the frequency spectrum of the impedance of the Windkessel model simulates the average characteristics of the impedance of the natural arterial tree reasonably well. Specifically, the similarity is better in the low-frequency range than in the high-frequency range. The fact that most of the oscillatory power of ventricular ejection resides in the first several harmonics suggests that the similarity of the impedance spectrum in the low-frequency range is more crucial than that in the high-frequency range. Therefore, we believe that the 3-element Windkessel model served the purpose of our analysis as a reasonable first approximation of the arterial input impedance. Influences of wave reflections in the natural arterial system on the optimal ventricular loading should be investigated in further studies.

**Appendix 1**

The slope ($E_o$) of the arterial end-systolic pressure vs. stroke volume relationship of the arterial system is determined by various factors. The following derivation of $E_o$, which is first a general form, and then
FIGURE 9. A schematic diagram of aortic pressure curve. The total area $A_T$ under the aortic pressure curve over one cardiac cycle $T$ is divided into $A_s$, the area over the systolic duration $t_s$, and $A_d$, the area over the diastolic duration $t_d$.

An approximation, will allow one to grasp the nature of $E_a$.

With reference to the afterload circuit of the model in Figure 1 and the schematic arterial pressure curve in Figure 9, mean arterial flow ($\bar{AF}$) averaged over the duration ($T$) of one cardiac cycle is obtained as

$$\bar{AF} = \frac{\bar{AP}}{R_e + R}$$

where $\bar{AF}$ and $\bar{AP}$ are aortic flow and arterial pressure averaged over one cardiac cycle. Since mean arterial flow equals $SV/T$, and mean arterial pressure equals the total area $A_T (= A_s + A_d)$ under the arterial pressure curve (Fig. 9) over one cardiac cycle divided by $T$, Equation 1 can be rewritten as

$$SV = \frac{A_T}{R_e + R}$$

Therefore, stroke volume can be related to $A_T$ and $R_e + R$ as

$$SV = A_T/(R_e + R).$$

The end-systolic pressure can be slightly different from the end-ejection pressure. However, if we disregard this small difference and denote both the end-ejection pressure and the end-systolic pressure by $P_{es}$, the diastolic pressure area $A_d$ in Figure 9 can be approximated by

$$A_d^* = P_{es} t_s [1 - \exp(-t_d/\tau)]$$

where $t_d$ is the duration of "arterial diastole" and is the time constant of the diastolic arterial pressure decay, which is equal to the product of the arterial resistance ($R$) and compliance ($C$). The asterisk indicates that Equation 4 is an approximation of the true $A_d$. Approximating the systolic pressure area ($A_s$) by the rectangle shown in Figure 9 yields an approximation of $A_s$ as

$$A_s^* = P_{es} t_e [1 - \exp(-t_d/\tau)]$$

where $t_e$ is the ejection time. Adding Equations 4 and 5 yields an approximation of $A_T (= A_s + A_d)$ as

$$A^* = P \left[ t_e + \tau [1 - \exp(- t /\tau)] \right]$$

The asterisk will be dropped hereafter. Substituting the approximate $A_T$ described by Equation 6 into the true $A_T$ in Equation 3 yields an approximated $P_{es} - SV$ relationship of the arterial system

$$P_{es} = \frac{R_e + R}{t_e + \tau [1 - \exp(-t_d/\tau)]} SV$$

and

$$E_a = \frac{R_e + R}{t_e + \tau [1 - \exp(-t_d/\tau)]}$$

If we further approximate the end-systolic pressure by mean arterial pressure, $P_{es}$ can be described as:

$$P_{es} \approx \frac{SV}{T}$$

where $R_T = R_e + R$. The effective arterial elastance $E_a$ defined as the slope of the $P_{es}$ vs. $SV$ relationship can then be first approximated by

$$E_a = P_{es}/SV = R_T/T.$$

This approximation indicates that the effective arterial volume elastance can be increased either by increasing the total arterial resistance or by decreasing the cardiac cycle length, whereas compliance has little effect unless it is changed excessively.

Appendix 2

The two capacitances in the inset of Figure 6 represent the reciprocal of ventricular end-systolic volume elastance $E_{es}$ and the reciprocal of effective arterial elastance $E_a$. Suppose that just before end systole, the right side capacitance is momentarily shunted to the ground, and at end-systole the switch momentarily closes to couple the two capacitances. Part of the energy stored in the ventricular capacitance will be transferred to the arterial capacitance, bringing the pressures in the two capacitances to an equilibrium. The energy received ($W_A$) by the effective arterial elastance at end systole is:

$$W_A = E_a SV^2/2.$$

The amount of volume shift from the left ventricle to the arterial system (i.e., $SV$) is simply determined by the ratio of $E_{es}$ to the sum of $E_{es}$ and $E_a$ as,

$$SV = \frac{E_{es}}{E_{es} + E_a} (V_{ed} - V_o)$$

where $V_{ed}$ and $V_o$ are the end-diastolic volume and the volume axis intercept of the ventricular end-systolic pressure-volume relationship, respectively. Substituting $SV$ in Equation 12 into Equation 11 yields,

$$W_A = \frac{E_{es} E_a^2 (V_{ed} - V_o)^2}{2(E_{es} + E_a)^2}.$$
equals $E_a$. Figure 6 illustrates this condition and the resultant maximal external stroke work of the left ventricle by the shaded area.

When $E_a = E_{es}$, Equation 12 simplifies to describe the optimized stroke volume as

$$SV_{opt} = \frac{(V_{ed} - V_o)}{2}, \quad (14)$$

namely, SV is 50% of effective preload (i.e., $V_{ed} - V_o$) in the optimally loaded condition.

**Appendix 3**

Substituting $E_a = E_{es}$ of Equation 10 and rearranging it yields

$$R_{T,opt} = E_{es}T, \quad (15)$$

which states that the optimal arterial resistance $R_{T,opt}$ is proportional to $E_{es}$ and cardiac cycle length $T$.

We gratefully acknowledge the excellent technical assistance of Kenneth Rent.

This study was supported in part by research grants from the National Institutes of Health, HL-14903 and Ischemic Heart Disease SCOR HL-17655.

Kenji Sunagawa’s current address is Research Institute of Angiocardiology and Cardiovascular Clinic, Kyushu University Medical School, Fukuoka, Japan.

Address for reprints: Kiichi Sagawa, M.D., Department of Biomedical Engineering, The Johns Hopkins University, School of Medicine, 720 Rutland Avenue, Baltimore, Maryland 21205.

Received July 30, 1984; accepted for publication January 16, 1985.

**References**


INDEX TERMS: Ventriculoarterial coupling • Impedance matching • Maximal external work • Optimal effective arterial elastance • Optimized ejection fraction
Optimal arterial resistance for the maximal stroke work studied in isolated canine left ventricle.

K Sunagawa, W L Maughan and K Sagawa

Circ Res. 1985;56:586-595
doi: 10.1161/01.RES.56.4.586

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/56/4/586