Responses of Left Ventricle to Changes in Aortic Input Impedance

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In order to evaluate how pressure and flow at the outlet of a ventricle are determined by the interaction between the ventricle and an aortic input impedance, we examined the effects of independent changes in the peripheral resistance and in the aortic compliance using isolated canine left ventricle preparations. There was an inverse linear relationship of mean values between pressure and cardiac output under pure resistance changes when coronary flow was maintained constant. But, when the coronary perfusion pressure depended on mean aortic pressure, the relationship was no longer linear under a critical aortic pressure.

When aortic compliance was increased, late systolic flow was enhanced and late systolic pressure decreased such that the stroke volume increased. The top part of the pressure-volume loop showed a configurational change from the right side down to the left side down. Changes in pressure and flow wave forms, and in the pressure-volume loop can be predicted by an electrical model in which time varying capacitance arranged in series with the internal resistance was used as a ventricular model.

STUDIES of isolated cardiac muscle revealed that the extent of shortening at a given initial muscle length was a function of the load against which the muscle attempted to shorten.¹ This load was termed an afterload. By analogy with cardiac muscle experiments, the aortic systolic pressure has been considered as the afterload against the left ventricle. However, the aortic pressure is determined as the product of an aortic input impedance and the aortic flow which is generated by the ventricle so the aortic pressure is not an extracardiac factor. The aortic input impedance is now considered to be the afterload against the ventricle.^{2,3}

Since the aortic flow and the aortic pressure are pulsatile, the aortic input impedance must be expressed as a frequency spectrum of moduli and

phases. If an electronic or hydraulic model which consists of a small number of elements has the same input impedance as the actual arterial system, we can substitute this model for the arterial system, and can examine how the ventricle behaves against changes in each element. In this paper, we first describe the development of such a hydraulic arterial model. Next, based on observations from isolated canine ventricle experiments, we show how the mean values of pressure and flow are determined under a given load. Then we show changes in pressure and flow wave forms, and changes in the pressure-volume loop under different aortic input impedances. Finally we present an electrical model which can mimic behaviours of the left ventricle against different aortic input impedances.

Key Words:

Aortic input impedance
Left ventricle
Aortic compliance
Coronary flow

METHODS

Aortic Input Impedance Model

A typical aortic input impedance spectrum

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Fig.1. Models of arterial system and its impedance spectrum. a) an example of the aortic input impedance, b) Windkessel model, c) three element model and d) four element model. Z = modulus of impedance; P = phase of impedance; C = aortic compliance; R_p = peripheral resistance; R_c = characteristic resistance; L = inertia

obtained from normal human subjects by Nichols et al.⁴ is shown in Fig. 1a). As shown in this figure, the modulus falls steeply from 0 to 2 Hz, and fluctuates with frequency thereafter. The phase angle approaches zero as frequency rises and becomes positive.

The first model to mimic the arterial system was the Windkessel model shown in Fig. 1b). This consists of two components, a peripheral resistance (R_p) and an aortic compliance (C). In the hydraulic model, a resistance can be realized by parallel capillaries, and its value can be adjusted by changing the available number of capillaries. A compliance can be realized by an air chamber, and its value can be adjusted by changing the air volume in the chamber. In this Windkessel model, however, the modulus approaches zero at high frequencies. Westerhof

Fig.2. Schematic drawings of the experimental setup.

a) isolated ejecting left ventricle preparation. LV = isolated left ventricle; Pr = reservoir for constant preload; L = inertia; R_c = characteristic resistance; C = aortic compliance; R_p = peripheral resistance; P = coronary perfusion pressure; LVP = left ventricular pressure; AoP = aortic pressure; AF = aortic flow
b) ventricular volume measurement system. CC = compensation chamber; DP = differential pressure transducer

et al. developed a three element model shown in Fig. 1c)⁵. They added another resistance which represents the characteristic resistance of the arterial system. In this model, the modulus reaches the value of the characteristic resistance at high frequencies, but the phase angle does not become positive at high frequencies. In our laboratory, Isoyama et al., adding an inertial part, developed the four element model shown in Fig. 1d)^{6,7}. The inertial element of the hydraulic model can be realized by a simple solid tube, and its value can be adjusted by changing the length of the tube. In this model, the modulus slightly increases and the phase angle becomes positive as frequency rises. At high frequencies, the four element model more closely resembles actual aortic input impedance than do the former two models.

Fig.3. a) relationship between cardiac output (C.O.) and mean aortic pressure (AoP). Open circles connected by solid lines were obtained under the constant coronary flow. Cross marks connected by intermittent lines were obtained under condition in which the coronary perfusion pressure was equal to the mean aortic pressure.
 b) Ho-Thévenin model. P_s = constant pressure source; R_i = internal resistance; R_L = load resistance
 c) graphical analysis for determination of cardiac output and the mean aortic pressure

Isolated Ejecting Canine Left Ventricle Preparation

Since a more detailed description of the preparation is given elsewhere,⁸⁻¹⁰ only a short description is presented here. Figure 2a) indicates the experimental design and apparatus. Both the left coronary artery and the right coronary artery of the heart, isolated from an adult mongrel dog, were cannulated and perfused with blood from support dogs. Heart rate was kept constant by electrical stimulation (90–140 beats/min). The perfusing blood temperature was maintained at 37°C with a thermostatic system. An aortic root of the isolated heart was connected to the four element hydraulic model described above. A wide cannula was inserted into the left atrium and connected to a large reservoir filled with saline. Thus the isolated left ventricle ejected saline against the hydraulic model without influencing coronary perfusion pressure. The left ventricular end-diastolic pressure was controlled by adjusting the height of the reservoir and kept at a constant value between 4–8 mmHg.

In some experiments, instantaneous left ventricular volume was measured with a pressure type plethysmograph as shown in Fig. 2b). The

isolated left ventricle which was enveloped with a thin unstressed latex balloon was set into a solid chamber, the volume of which was 3000 ml. Another chamber with the same volume was used to compensate for the influence of the ambient temperature. Volume changes in the left ventricle were measured as pressure difference between the two chambers.

RESULTS

Relationship between Mean Aortic Pressure and Cardiac Output

Open circles in Fig. 3a) show the relationship between mean aortic pressure and the cardiac output obtained under different peripheral resistances. As shown in this figure, there was a linear inverse relationship between these parameters.

The above data were obtained under the condition of constant coronary flow, but in situ the perfusion pressure to coronary circulation is determined by the aortic pressure. To duplicate this situation, the perfusion pressure to coronary circulation was adjusted to the same level as the mean aortic pressure under each peripheral resistance. In this variable coronary flow con-

Fig.4. Left ventricular pressure and aortic flow under different peripheral resistances (left panel) and under different aortic compliances (right panel). Values of resistance are expressed in $\times 10^3$ c.g.s units and values of compliance are expressed as air volume in Windkessel. Arrows indicate the time of the dicrotic notch in aortic pressure.

dition, reduction of peripheral resistance decreased the mean aortic pressure in qualitatively the same manner as in the constant coronary flow condition. Reduction of the peripheral resistance to a certain level increased the cardiac output, but further decrease of the peripheral resistance resulted in a decrease of the cardiac output rather than an increase.¹⁰ Cross marks in Fig. 3a) show the relationship between the mean aortic pressure and the cardiac output under the variable coronary flow conditions. As shown in this figure, the cardiac output decreased when the mean aortic pressure was below a critical level.

Changes in Pressure and Flow Wave Forms

The left panel of Fig. 4 shows superimposed left ventricular pressures and aortic flows under four different peripheral resistances. The right panel shows these same quantities under four different aortic compliances. As the peripheral resistance was reduced, left ventricular pressure showed a parallel downward shift, and aortic flow during early systole increased. In contrast,

Fig.5. Pressure (LVP)-volume loops under different peripheral resistances (a) and under different aortic compliances (b).

when the aortic compliance was increased, early systolic left ventricular pressure slightly increased and late systolic pressure decreased. Peak aortic flow increased and occurred later. Thus the late systolic flow was enhanced by an increase in aortic compliance.

Changes in the Left Ventricular Pressure-Volume Loop

Fig. 5a) shows left ventricular pressure-volume loops obtained under different peripheral resistances. Reduction of the peripheral resistance decreased the pressure during the ejection phase and decreased the end-systolic volume. Reduction of pressure during the ejection phase seems parallel.

Fig. 5b) shows left ventricular pressure-volume loops obtained under different aortic compliances. The changes in these loops are somewhat complex. By increasing aortic compliance, end-systolic volume decreased, so that stroke volume increased, since the end-diastolic volume was kept constant. The right half of the pressure during the ejection phase was increased by the increase in aortic compliance. The left half of the pressure during ejection phase decreased, so that the configuration of the top part of the loop changed from left side up to right side up by the increase in aortic compliance.

DISCUSSION

Pumping Characteristics of the Left Ventricle in Terms of Steady Pressure and Flow

How are the mean values of aortic pressure and cardiac output (= mean aortic flow during a minute) determined by the interaction between the aortic input impedance and the left ventricle? Generally the characteristics of a pump can be expressed by the relationship between pressure and flow at its outlet ("pump function graph"). As shown in Fig. 3, in the case of the left ventricle, the pump function graph expressed by the mean aortic pressure and the cardiac output shows an inverse, almost linear, relation. This pump function graph can be analysed by a Ho-Thévenin model in which a constant pressure source (P_s) is arranged in series with an internal resistance (R_i) as shown in Fig. 3b). This model is widely used to describe the characteristics of an electrical generator. In the plane of the mean aortic pressure and the cardiac output as shown in Fig. 3c), the pressure generated by a constant pressure source corresponds to the

pressure axis intercept, and the value of internal resistance corresponds to the negative slope of the pump function graph. Since the relationship between pressure and flow across the load resistance obeys Ohm's law, it is represented by an intermittent line in Fig. 3c). Thus the mean aortic pressure and the output under a certain load resistance are determined by the crossing point of these two lines. It is obvious that the pressure generated by the constant pressure source corresponds to the mean pressure generated under isovolumic contraction, and the load resistance corresponds to the total systemic resistance. But the physiological meaning of the internal resistance has not been clearly documented. Elzinga and Westerhof reported that the slope of the pump function graph was increased with a parallel increase in contractility, but was not altered by regional ischemia^{11,12}. It should be noted that the analyses mentioned above are valid only in the condition of pure resistance change. If the aortic compliance changes concomitantly, the relationships between the mean aortic pressure and the cardiac output deviate from the pump function graph. To overcome this problem, Elzinga and Westerhof suggested use of the mean left ventricular pressure instead of the mean aortic pressure as pressure parameter.¹¹⁻¹³

Under conditions where the perfusion pressure to coronary system depends on aortic pressure, the relationship between mean aortic pressure and the cardiac output deviates downward when the mean aortic pressure is below a certain level. Thus the pump function curve of a ventricle in situ is expected to be curved below a certain mean aortic pressure level.

Changes in Pressure and Flow Wave Forms

As shown in Fig. 4 left panel, changes in peripheral resistance did not induce apparent changes in the pressure wave form while the amplitudes of the pressures were markedly changed. In contrast, changes in the aortic compliance altered the pressure wave form during the ejection phase; the high compliance load enhanced early systolic pressure and the low compliance load enhanced late systolic pressure. It has been observed clinically that the ratio between arterial pressure during the early ejection phase and that during the late ejection phase may reflect the elasticity of the arterial system.¹⁴ Generally this changes in pressure wave form has been attributed to the enhanced

Fig.6. Electrical model for simulation of the interaction between left ventricle and arterial system.

Fig.7. Results of simulative changes in peripheral resistance. Left upper panel; ventricular pressure (LVP), left lower panel; aortic flow (FLOW), right upper panel; pressure-volume loop, right lower panel; flow-pressure loop. Control value (C) is listed in the appendix.

reflection of the pressure wave from the periphery.¹⁵ However, in our hydraulic model, there is essentially no reflection. Thus, such configurational changes in the pressure wave can be induced, at least in part, by changes in aortic compliance. These changes in pressure wave form induced by an alteration of aortic compliance have been noted by several investigators

in a variety of preparations.^{13, 16-18}

The pressure-volume loop changes in response to changes in the pressure and flow wave forms, by alteration in aortic compliance (Fig. 5b). It appears that the increase in stroke volume induced by the increase in aortic compliance is due to the decrease in late systolic pressure.

Fig.8. Results of simulative changes in aortic compliance.

Fig.9. Results of simulative changes in characteristic resistance.

Electrical Model

It is not easy to understand and predict how pressure and flow wave forms are determined by the interaction between the left ventricle and the aortic input impedance. We attempted to build a model which could demonstrate the action of a left ventricle against the aortic input impedance.

For the model of a left ventricle, we employed principally the time varying capacitance model, established experimentally by Suga et al.¹⁹ However, it has been reported that the

instantaneous pressure during the ejection phase is slightly below that which is expected from the time varying capacitance model because of the viscous nature of a ventricle.²⁰ To compensate for this factor we added a resistance in series with the time varying capacitance. From the flow pulse method carried out by Hunter et al.^{21,22} the volume perturbation method of Templeton et al.²³ and the forced vibration method of Koiwa et al.²⁴ it has been suggested that the value of this resistance relates in a linear

function to the ventricular pressure. Thus, we employed the model shown in left part of Fig. 6. For the arterial system, we employed a three element rather than a four element model to avoid complexity arising from the existence of the inertial element. Given values to parameters are obtained primarily from an experiment by Shroff et al.²⁵ and listed in the appendix. A microcomputer (NEC 8801), was used to calculate the differential equation which describes the model and was repeated until a steady state of pressure was obtained.

Figure 7 shows the results of peripheral resistance change. It should be noted that with the reduction of the peripheral resistance, the following particular characteristics observed in isolated ventricles can be predicted: 1) a parallel downward shift of pressure during the ejection phase in the time domain, 2) a parallel shift of pressures in the pressure-volume plane and 3) enhancement of early systolic aortic flow.

Figure 8 shows the results of aortic compliance change. With the increase in aortic compliance, the following particular characteristics observed in the isolated ventricle can be predicted: 1) decrease in late systolic pressure, 2) enhancement of the late systolic aortic flow and 3) decrease in the end-systolic volume.

Thus, the model shown in Fig. 6 seems to be applicable and useful in examining the interaction between the left ventricle and the aortic input impedance. While we did not examine the effect of the characteristic resistance in the isolated ventricle, analyses of the model can predict it. Fig. 9 shows the results of characteristic resistance change in this model. These results predict that reduction of the characteristic resistance will decrease peak systolic pressure and enhance early systolic aortic flow.

In summary, based on the electrical model, changes in the peripheral resistance mainly affect the amplitude of the pressure and the flow, and the changes either in the aortic compliance or in the characteristic resistance affect pressure and flow wave forms.

APPENDIX

In the model shown in Fig. 6, the pressure-flow-volume relationship of the ventricle can be described by the following equation:

$$LVP(t) = E(t) (V(t) - V_d) - R_i \times F$$

where $E(t)$ is the time-varying slope coefficient of the regression line of instantaneous pressure

($LVP(t)$) on instantaneous volume ($V(t)$), and V_d is the volume axis intercept of the end-systolic pressure-volume regression line. F is the aortic flow and R_i is the internal resistance, which is a function of pressure as follows;

$$R_i = k_1 + k_2 \times LVP(t)$$

In this simulation, we represented $E(t)$ with following polynomial;

$$E(t) = k_3 + k_4 \times t + k_5 \times t^2 + k_6 \times t^3$$

Values of V_d and the coefficient k_1 – k_6 were taken from the experimental results of Shroff et al. as follows; $V_d = 5.1$, $k_1 = -0.247 \times 10^{-2}$ mmHg ml⁻¹s, $k_2 = 0.123 \times 10^{-2}$ s ml⁻¹, $k_3 = 0.42$, $k_4 = 2.2$, $k_5 = 171$, $k_6 = -536$. As the control load, we give following values to each element of the three elements arterial model; $R_c = 0.225$ mmHg ml⁻¹s, $R = 6$ mmHg ml⁻¹s, $C = 0.16$ ml mmHg⁻¹.

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