Interaction of Left Ventricular Contraction and Aortic Input Impedance
in Experimental and Clinical Studies

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Implication of aortic input impedance and left ventricular coupling were
investigated in three series of studies. In a clinical study, the ascending
aortic flow velocity and pressure were simultaneously recorded from a
multisensor catheter, and input impedance was calculated from 8 harmonics
of aortic pressure and flow. Left ventricular wall stress was calculated from
diameters and wall thickness of cineventriculogram and simultaneous
recording of left ventricular pressure. In the experimental study, program-
mable artificial pulsatile pump was used to control pulsatile blood flow in
dogs.

The pressure-flow relationship in the arterial system had slightly convex
curves toward the pressure axis with a critical turning pressure, so the arterial
system had low output — high resistance and high output — low resistance
characteristics. Therefore, the failed heart should inevitably eject the blood
against stiffened vascular beds. Increased work load of the ventricle as
expressed by sustained ventricular wall stress was determined mainly by the
exaggerated late systolic pressure due to increased input resistance and
increased low frequency pulsatile component of the input impedance. These
findings are especially important for relieving additional work load of the
ischemic heart, which have higher pressure wave reflection.

The left ventricle ejects the blood into the arterial system and the ejected blood
generates a pressure wave with an interaction of the arterial system. It is physiologically divided
into conduit vessels and resistant vessels, and the mean pressure is relevant to peripheral resistance
and the pulse pressure around the mean pressure to properties of conduit vessels and cardiac
contraction. A generated pressure wave in the ascending aorta propagates rapidly to the per-
ipheral arteries, there some of the pressure wave is reflected back to the aortic root and merges to
the forward pressure. The contour of the left ventricular outflow velocity is almost the
same even in the ischemic heart; therefore the wave shape of the arterial pressure recorded in
the ascending aorta is mainly characterized by properties of both large arteries and resistant
vessels with pressure wave reflection. We can inclusively express all these components of the
vascular resistance as the aortic impedance, a concept which was introduced by Wormersley
and Mc Donald.

Key Words:
Aortic input impedance
Total systemic resistance
Left ventricular wall stress
Pressure wave reflection

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Nowadays, the left ventricular load is defined simply as the time varying ventricular pressure. During isovolumic contraction, the left ventricular load is increasing with rising ventricular pressure, however, once the aortic valve opens, the left ventricle meets the aortic pressure. Because of very short isovolumic period, it is reasonable to say that the left ventricular afterload is characterized for the most part by the aortic input impedance. This study summarized several issues: (1) what is the effect of the pressure-flow relationship (the input resistance) on the left ventricle? (2) what elements in the arterial system characterize the left ventricular load (stress)? (3) does the pressure reflection wave have a deleterious effect in ischemic heart disease and hypertension?

METHODS

1. Experimental study

Experiments were performed on 4 adult dogs, weighing between 16 and 21 kg (mean 18.5 ± 2.1 kg). After anesthetizing with sodium pentobarbital (20 mg/kg), the trachea was intubated and ventilation with 100% O₂ gas was performed with a positive-pressure respirator. A sternum thoracotomy was done and the pericardium was opened. Flow was measured with a gated sine-wave electromagnetic flowmeter at the aortic root and pressure was measured by means of Millar’s catheter tip transducer (PC-350) inserted from the right carotid artery. After recording control level of the aortic flow and pressure, a Harvard pulsatile pump (model 1421) was provided to the dog for the control of cardiac output. This model of the pulsatile pump can regulate stroke volume from 0 to 35 ml, heart rate from 10/min to 200/min and output phase ratio (systole to total one cycle) from 30% to 70%. The right and left arterial appendages were cannulated and connected with 5% dextran solution to the venous return line. The oxygenator and the pump were connected with a tube, and a polyethylen tube, 1.7 cm in diameter and 50 cm in length was provided for the pump flow. After fibrillating the heart, the tube from the pump was inserted from the apex of the left ventricle and positioned just below the aortic valve. The time to start the pump flow after fibrillation of the heart was within 17 sec. Based on the control level of the cardiac output of canine heart, the pump flow rate in the control condition was set as follows; stroke volume 10 ml, heart rate 135/min, and outphase ratio 50%.

Two different series of experiments were carried out. In the first set, aortic flow was changed in steps from 2.43 L/min by the pump in the combination of three different stroke volumes (5, 10 and 15 ml) and four different heart rates (90, 115, 133, and 158/min). In the second group of experiments, the ejection ratio against the pump cycle was changed in 5% steps from 35% to 65% at the different but fixed heart rate and stroke volume. During two series of experiments, the dogs were observed with their hearts fibrillated and cardiac nerves intact. Blood level of the reservoir of the oxygenator was kept constant, so circulatory blood volumes in the dogs were assumed to be constant. All aortic pressure were recorded (TEAC 71).

2. Clinical study

Three different sets of clinical studies were conducted. The first study group included two patients, the second twenty two, and the third thirty, all of them were catheterized for various clinical indications. In each study, the measurements of instantaneous left ventricular and aortic pressures and aortic flow velocity was made with a #8 French multisensor catheter (Millar VPC 684D) during diagnostic left heart catheterization. The electromagnetic velocity and high fidelity pressure sensor located 5 cm from the tip of the catheter were positioned near the upper border of the sinus of Valsalva. Thermodilution technique was introduced to measure
cardiac output of the right heart by using Swan Ganz catheter. The flowmeter was operated with a square wave electromagnetic flowmeter (Carolina Medical Electronics Model 501) and signals amplified with Electronics for Medicine amplifiers (Model VR16). Flow signals were low-pass filtered with corner frequencies at 30Hz. Physiological evaluation of the flowmeter was conducted to test (1) output voltage and flow velocity, (2) time lag of the flow velocity system, (3) effect of hematocrit (4) effect of temperature. After connecting to the flowmeter, a catheter was directed up and down sinusoidally in the blood samples of various hematocrit and temperature by the variable speed motor. Outputs from a catheter and the displacement meter (Helipot 8342M) in various conditions were recorded and analysed following to Mill's method. The motor

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delivered flow velocity up to 120 cm/sec, and the calibration line or the sensitivity of the flow probe (measured velocity/output voltage) was calculated by the determination of the straight line through the individual average values at five steps. The deviation from a straight line was less than ±7% up to 100 cm/sec, independent of hematocrit and temperature. An increase of the hematocrit values from 21% to 53% in five steps decreased the sensitivity of the probe, while an increase of the temperature from 21°C to 38°C in five steps increased the sensitivity. The sensitivity of the probe and the influence of the hematocrit were different in each catheter. Time delay of the flow velocity system was linear up to 100 cm/sec and 10, 5, and 2 msec respectively operating at 100 cm/sec in each 10, 30 and 100Hz of low pass filter.

Changes in the diameter of the upper margin of the sinus of Valsalva were considered negligible. So that aortic mean flow was calculated from the flow velocity signal and the aortic root area on cine films. Figure 1 compared the stroke volume derived from the thermodilution method and that from the aortic flow velocity signal. The correlation was high (r = 0.97), but stroke volume of the flow velocity probe were somewhat smaller than that of thermodilution.

All signals were recorded on analog magnetic tape (SONY OFR 71460A or TEAC 71) and also paper tape preparation of the recorder (Electronics for Medicine VR 16). Aortic pressure and velocity signals were digitized at a sampling interval of 5 msec by analog to digital converter or sonic pen by hand (Model 3500P-B, NAC, Tokyo). Following the method outlined by Mc Donald the aortic input impedance was calculated by aortic pressure and flow data which were converted to a Fourier series as a function of frequency, was represented as pressure/flow amplitude and pressure-flow phase spectra. The input impedance was calculated as the ratio of mean pressure and mean flow, and characteristic impedance (Zc) was calculated as the arithmetic mean of impedance moduli over 2 Hz. For impedance determination, results were averaged over three to eight pulses to cover one respiratory cycle.

Stress was defined as the left ventricular wall force per unit cross-sectional area, and for its calculation, Mirsky's formula was used. Left ventricular cineangiography was performed in the 30° RAO position using a side hole catheter.

Fig.4. Pulse pressure from both peak aortic pressure and pressure at incisula (A2 pressure) to diastolic pressure plotted as a function of ejection duration of programmed artificial pump.

Fig.5. Effects of low frequency moduli in aortic impedance on the left ventricular stress in patients. Triangle, circle and square indicate patients with left ventricular volume below 110 ml, from 111 to 130 ml, and from 131 to 150 ml respectively. See text about normal and sustained stress pattern.
on the top of which pressure sensor was attached (Miller type 481). Films were exposed at a rate of 150 frames per sec with a 35 mm Aritecno cine camera mounted on a Siemens 7 inch image intensifier. Newly developed equipment for left ventricular edge follow computation was used (Model 3500P-B, NAC). Values of left ventricular dimensions with wall thickness and corresponding left ventricular pressures were calculated and constructed into a single stress curve of one cardiac cycle.

RESULTS

1. Input resistance, cardiac output and mean blood pressure

The relationship between arterial blood pressure and cardiac output generated by the artificial pump in four dogs is shown in Fig. 2. The three sets of parallel lines represent systolic and diastolic pressures at each corresponding cardiac output generated by constant stroke volume of 5, 10, and 15 ml with each four different heart rate of 94, 118, 140 and 158
beats/min. If mean pressure and mean flow relation is fitted visually in the middle series, which can be approximated as normal values, the line has a pressure intercept of 40 mmHg. Above the physiological range, pressure-flow relation had an almost linear line but less steeper slope. Below normal flow level, on the other hand, pressure/flow line was non-linear, and at the point of 0.6 L/min the slope turned toward 0.

In the clinical study two patients with slow heart rate received cardiac pacing under aortic flow and pressure monitoring with a multisensor catheter. Arterial mean pressure and calculated cardiac output from aortic flow velocity under four or five different cardiac pacing are shown in Fig. 3. A visually fitted straight line of pressure and flow relation intercepted around 60 mmHg on the pressure axis in two patients, although the pressure/flow slope in hypertension was steeper than that of normal pressure. After propranolol 6 mg and atropin sulfate 2 mg intravenous administration, the slope appeared to be the same.

2. Interaction of left ventricular contraction and arterial system

If the contraction of the left ventricle is similar then the properties of the arterial system should reflect on the pressure wave shape. On the contrary, if the arterial system is almost constant in physiological state, the form of left ventricular contraction reflects on the pressure wave shape. Effects of duration ejection of artificial pump on the pressure wave shape in four dogs were shown in Fig. 4. These results could be explained by less stiff aorta in dogs and better matching of arterial system which cancels reflection wave from the upper and lower body of the dog as compared with human! There were no significant changes in pulse pressure and pressure shape in the physiological state. These findings were also true in other conditions of different stroke volumes and different heart rates.

The effects of low frequency moduli of aortic impedance on the left ventricular stress curves were studied in twenty two patients. Diagnoses were primarily chest pain syndrome and ischemic heart disease. No valvular incompetence was detected and left ventricular volume was below 150 ml and ejection fraction was above 50% in each patient. The mean value of impedance moduli from one to three harmonics was adopted as an index of afterload. This index includes more than 70 percent of pulsatile component of pressure flow relation and it expresses both the characteristic impedance of the aorta and reflection wave from the peripheral arteries. Normal stress pattern indicates that the duration of fifty percentile of the peak stress is less than half of the duration ejection; on the other hand sustained stress pattern shows its duration is more than half of the duration ejection. In nine patients with normal stress, the pattern im-
pedance moduli of low frequency was 82.6 ± 12.8 dyne·sec·cm⁻⁵ and that of thirteen patients with sustained stress pattern was 130.1 ± 39.5 (p < 0.01). The average ages in normal and sustained stress groups were 46 and 48 years (N.S.), the mean blood pressures in both groups were 114 and 96 mmHg (N.S.) and input resistance was 1369 and 1863 dyne·cm·sec⁻⁵ (p < 0.05).

3. Pressure wave reflection in ischemic heart disease and hypertension

The subject group included thirty patients. Six subjects had no cardiovascular disease, seventeen had ischemic heart disease and seven had established hypertension. Ages and mean arterial blood pressure were given in Fig. 8. A simple method to evaluate reflection pressure wave ratio on systolic pressure wave shape of the ascending aorta was introduced in this study. Measurement of reflection wave ratio (P₁P₂ / P₀P₂) was explained in Fig. 6. To observe the proprieties for reflection wave ratio, the absolute mean values of the difference from characteristic impedance between one to eight harmonics \( \Sigma_{n=1}^{8} |Zc-Zn|/8 \) was calculated. The relationship between reflection wave ratio and \( \Sigma_{n=1}^{8} |Zc-Zn|/8 \) in seventeen patients are shown in Fig. 7. Mean value of reflection wave ratio was 29.7 ± 12.6 percent in subjects without heart disease, 37.8 ± 15.9 in ischemic heart disease, and 55.9 ± 13.5 in hypertension (Fig. 8).

DISCUSSION

The input resistance, or the resistive component of systemic impedance, is calculated by relating the mean pressure and mean flow at the input of the arterial system. Under the condition of right atrial pressure close to zero, the input resistance has the same meaning as the total systemic resistance. The peripheral resistance is also calculated by relating mean flow and pressure difference between peripheral artery, whose pressure is only two or three mmHg below the mean aortic pressure and the capillary vein. Therefore, it is also acceptable to use the input resistance in place of the peripheral resistance.

As shown in Fig. 2 and 3, resistance vessels have characteristics of the pressure-flow relation which can be approximated by slightly convex curves toward the pressure axis. The input resistance is the slope of the line connecting mean arterial pressure-cardiac output data to the origin of the graph, so the slope in our two series data are steeper at the low cardiac output and lower at the high cardiac output. In Fig. 2 the results of the pressure-flow relation in a range from 55 ml/min·kg to 95 ml/min·kg of the flow agree with the observation by Sagawa and Eiser who demonstrated the pressure-flow line which had a slope of 0.60 and a pressure intercept of 40 mmHg (40%) if control level of pressure was 100 mmHg (100%). In the set of stroke volume 15 ml experiment, the pressure-flow relation was also linear but the slope of this relation was less steep than the data of Sagawa et al.. This finding could be result of the baroreflexes responding to a rise in arterial pressure by the large stroke volume to produce peripheral vasodilatation.

After administration of propranolol 6 mg and atropin 2 mg for the study of sinoatrial node function in two patients (Fig. 3), we tried to demonstrate the pressure flow relation under the different baroreflex condition in the arterial system presented as dotted lines in Fig. 3. However compared with the control level, the slope of the pressure-flow relation seems to be similar and the pressure axis intercept was approximately 60 mmHg except one condition of low cardiac output after using the blockers in 58 years old male case. The dosage of the blockers in our study was less than that of the other study for evaluating the baroreflexes in hypertension, so further clinical studies are needed for evaluating the arterial properties after denervation in pharmacological blockade.

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In Fig. 5, we try to demonstrate that the time course, not absolute value, of cardiac work load (stress) is determined mainly by low frequency pulsatile component of the input impedance. Wall stress curve during ejection is a function of both systolic increase in aortic pressure and systolic decrease in left ventricular volume with parallel increase in wall thickness. However, stress pattern should mainly depends on the arterial pulse pressure with changes in wave shape, since twenty two patients in this series had normal left ventricular volume with normal wall thickness and normal aortic flow velocity pattern as well. From the study of expressing arterial properties by input impedance, the mean value of impedance moduli between one to three harmonic components covers more than 70% of total pulsatile component in pressure-flow relation, and the amplitude of harmonics of ascending flow waves is increased mostly in the first three harmonics. Therefore it appears that an optimal relationship exists between the left ventricular contraction and the left ventricular work load which is apparent when the impedance moduli is lower at the low frequency.

Input resistance was also significantly increased in the sustained stress group. Increased input resistance as measured by a rise in vascular tone of resistance vessels increases reflection coefficient of the pressure wave as well as the mean blood pressure. A rise in mean pressure increased arterial stiffness that increases pressure pulse wave velocity. Sustained type of stress pattern is thereby caused by an augmented reflection wave returning early to systole due to increased peripheral resistance and arterial stiffness. It is clearly demonstrated in Fig. 6 that augmented late systolic peak during reduced ejection period or decelerated flow velocity phase has strong effects on the pattern of the stress curve.

The integrated left ventricular wall stress curve during systole is accepted as one of the major determinants of the myocardial oxygen demand. However, even if the integrated wall stress is the same, the sequence of increasing afterload during systole could affect the myocardial energy consumption process, and this sustained ill effect on the myocardium could cause left ventricular dysfunction as a consequence. This idea coincides with the previous data reported by the author in which left ventricular stress maintained a high level during ejection in patients with chronic left ventricular dysfunction, while the corresponding volume distensibility of the ascending aorta remained at the same level with normal left ventricular function.

Murgo et al. showed that pressure wave of the adult patients recorded in the ascending aorta was characterised by a notch in the mid part of systole and a secondary wave in the late. They identified this secondary wave as a result of wave reflection. A simple method for detecting reflection wave ratio to total pulse pressure (P1P2/P0P2) was proposed in this paper. This index had a reasonable correlation (r = 0.654, p < 0.005) to the mean value of reflection components of the moduli between one to eight harmonics in the ascending aorta (Fig. 7). It should be especially useful for detecting additional work load to the heart or for demonstrating the relief of the load after arterial vasodilation therapy, if we could examine noninvasively pulse wave and doppler flow velocity tracings on the carotid arteries.

The exaggerated late systolic peak is apparent in hypertension (Fig. 6), and almost upper fifty percentile of the pulse pressure is consisted of the reflection wave (Fig. 8). Reflection wave ratio in ischemic heart disease is higher than that of normal heart subjects. There was no statistical significance between them, but if the number of the normal heart subject was a little higher, the difference should be apparent. Increased reflection wave in ischemic heart disease is compatible with the data from Nichols et al. in which ischemic patients with increased characteristic impedance showed evidence of early return to wave reflection. As a result of early return of the reflection wave, increased systolic peak occurs in late systole and diastolic pressure decreases earlier. This phenomenon in the ischemic heart negatively affects left ventricular work by sustained left ventricular wall stress and coronary blood flow by decreased perfusion pressure. We could understand the vasodilation therapy for the ischemic heart from the stand point of improving and relieving cardiac performance both by decreasing and delaying wave reflection and by decreasing systolic pressure and maintaining diastolic pressure as a result.

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