The Pumping Ability of the Left Heart and the Effect of Coronary Occlusion

GUS ELZINGA, M.D., PH.D., AND NICOLAAS WESTERHOF, PH.D.

SUMMARY In an isolated preparation of cat heart we studied the pumping capacity of the left heart while left atrial filling pressure was kept constant. We used the source impedance concept to quantify the pumping capacity. In this source impedance concept the relation between left ventricular output and left ventricular pressure is given by the formula

\[ Z_s(\omega) = \frac{P_{lv}(\omega) - P_{a}(\omega)}{I_{lv}(\omega) - I_{a}(\omega)} \]

where \( Z_s \) = source impedance, \( P_{lv} \) = left ventricular pressure, \( I_{lv} \) = flow in the ascending aorta, and \( \omega = 2\pi f \), \( f \) being frequency. The pressure obtained at zero flow is called the hydromotive pressure (HMP). Only the mean values of pressure and flow were studied. We studied the behavior of 10 hearts in three different experimental situations and in the following sequence: (1) control conditions, (2) after ligating a part of the left coronary arterial system, and (3) after restoring left ventricular output to control level by raising left atrial filling pressure. It was found that source resistance was not significantly different in the three situations but that mean hydromotive pressure (HMP) was significantly lower after ligation of a part of the left coronary arterial system. It was concluded that the decrease in pumping capacity of the left heart after infarction can be compensated for almost completely by an increase in left atrial filling pressure. This compensating mechanism therefore seems to be very efficient.

Our present investigation was made on an isolated ejecting cat heart preparation. We have concentrated mainly on the left ventricle, namely, the source impedance and the effect of coronary occlusion. This was done by increasing left atrial filling pressure and, consequently, left ventricular end-diastolic volume.

Methods

ISOLATED EJECTING CAT HEART PREPARATION

Since a more detailed description of the preparation is given elsewhere, only a short description is presented here.

Figure 2 shows the experimental arrangement used for the isolated ejecting cat heart. The large reservoir (R) contains an oxygenated mixture of Tyrode's solution and washed bovine erythrocytes. The hematocrit of the mixture is 25, hemoglobin concentration is 8.6 g/100 ml, pH varies between 7.39 and 7.43, PO₂ between 125 and 300 mm Hg, and PCO₂ between 25 and 30 mm Hg. The temperature of the fluid, when offered to the left atrium, is 37.5 ± 0.3°C. Temperature control is achieved by pumping warm water through a coil suspended in the perfusion fluid. The pump is controlled by a thermistor that continuously measures the temperature in the reservoir R.

The perfusion fluid in the reservoir R is under pressure and it is forced, via a filtering device (F), to a left atrial supply container (SL). The height of the fluid in SL is controlled by an overflow vessel (OL); the overflowing volume is pumped back from the small reservoir (RL) into...
FIGURE 1 Electrical analog of the arterial part of the systemic circulation and the left side of the heart. HMP = generator pressure of hydromotive pressure; \( P_{lv} \) = left ventricular pressure; \( I \) = the blood flow through the system; \( Z_s \) = the source impedance; and \( Z_o \) = the input impedance of the arterial system. The latter system is composed of three elements: \( R_c \), which models the characteristic impedance of the first part of the ascending aorta; \( C \), which mimics the total arterial compliance and \( R_p \), which is comparable with the peripheral resistance.

The large reservoir \( R \). The connection of SL with the left atrium is short and has a large bore to keep effects of fluid inertia on cardiac filling small. The time needed for acceleration of the fluid is less than 50 msec.

The left ventricle ejects its contents into a hydraulic model of the input impedance of the systemic arterial tree of the cat. Use of this "loading system" results in patterns of aortic flow and pressure which closely resemble the shapes of those variables recorded in vivo (Fig. 3). The resistor \( R_c \) is equivalent to the characteristic impedance of the first part of the ascending aorta. The capacitance \( C \), representing the total arterial compliance, can be changed by changing the air volume under the piston. The peripheral resistance \( R_p \) can be changed by moving a slide that closes the desired number of the many tiny conduits of which the resistor is composed. The slide is moved by a servomotor.

FIGURE 2 Layout of the experimental setup. R is a big reservoir containing an oxygenated red cell Tyrode's mixture, F is a filter, SL is the left atrial supply vessel where the height of the fluid is kept constant by the overflow system, OL, and RL is a small reservoir from which overflowing fluid is pumped back into R. The isolated cat heart is loaded with a hydraulic model of the input impedance of the arterial system of the cat. \( R_c \) is a hydraulic resistor, \( C \) is a capacitor (total arterial compliance), and \( R_p \) is the peripheral resistance. Cardiac output \( I \) is measured by collecting fluid in a glass cylinder. Instantaneous blood flow \( I_{in} \), aortic blood pressure \( P_{ao} \) and left ventricular blood pressure \( P_{lv} \) are measured as well.

Isolated cat hearts were obtained from male cats; the weights of the hearts ranged from 15.7 to 26.2 g (n = 10). The cats were anesthetized with sodium thiopental (45 mg/kg) administered intraperitoneally (ip). Under artificial ventilation the heart was taken out of the thorax and connected to the input and output of the system described above. During the time needed to connect the heart to the experimental setup it was kept perfused by the Langendorff technique to continue coronary perfusion. When connections were complete the left ventricle ejected its content into the hydraulic model and generated its own coronary perfusion pressure. The experiments were started about 20 minutes after the heart had been taken out of the animal.

INSTRUMENTATION AND MEASUREMENTS

During the experiments we recorded aortic pressure, left ventricular pressure and aortic flow (Fig. 3). Pressures were measured through stiff polyvinyl chloride tubing, 30 cm in length, and Statham 23 Db pressure transducers. Aortic pressure was measured as lateral pressure. Left ventricular pressure was measured through a needle stitched into that cavity at the apex. The damped resonance frequency of the systems was 80 Hz. Aortic flow was measured electromagnetically with a Biotronex BL-610 pulsed-logic flowmeter. The frequency response of this system was 3 dB down at 100 Hz; time delay was 2.3 msec.

Since the calculation of the source resistance involves subtraction of large quantities (see Eq. 3), accuracy of measurement has to be high in order to obtain a reliable answer. Therefore we determined mean flow by collecting the amount of perfusion fluid ejected by the left ventricle during 30 seconds. The amount of the fluid collected was determined by weighing.

Left ventricular pressure (the mean of which being the other variable needed to calculate source resistance) was
averaged by an analog filter (KEMO VBF/3; setting: -6 dB at 0.5 Hz and a fall-off of 48 dB per octave). The mean left ventricular pressure so obtained was, after calibration, measured with a digital voltmeter. Data also were recorded on an Elema Schönander direct-writing system (EMT 81) and on magnetic analog tape (Hewlett-Packard 3525A).

EXPERIMENTAL APPROACH

As described in the introduction, two settings of the loading system are enough to determine the source resistance and the generator pressure; however, use of more settings of the loading system gives the advantage of increased accuracy.

In the experiments reported here we changed the setting of the loading system by changing the peripheral resistance of the hydraulic model; the capacitance was kept constant during the experiments. We avoided low aortic pressures and small aortic flows, trying to study performance over a reasonable working range. At each setting of the peripheral resistance we measured mean ventricular pressure and mean aortic flow. No measurements were made during transient states. We always waited 15-20 seconds after an intervention to make measurements. The values obtained were plotted against one another. Examples of these plots are shown in Figures 4 and 9. The slope of the line which can be drawn through these points is the source resistance (ΔPm/ΔQao) (see Eq. 3) and the intercept with the ordinate represents the mean hydromotive pressure (HMP).

The actual experiments ran as follows: After preparation of the isolated cat heart we started the experiment by establishing the control condition: left atrial filling pressure of about 4 cm H2O, mean aortic pressure of 80 mm Hg, heart rate fixed by left atrial pacing. We then increased the peripheral resistance in steps. When flow had fallen to about 1.5 cm3/sec the resistance was lowered, again in steps, to the control value. When this "run" appeared to be stable, i.e., when the control values for pressure and flow obtained before and after resistance changes did not differ more than 5%, the lower part of the descending branch of the left coronary artery was tied off. This resulted in a decline in the function of the heart. During this decline, mean aortic pressure was kept at 80 mm Hg by changing the peripheral resistance, but left atrial filling pressure was kept constant. When the heart had stabilized at a lower level of mechanical activity we repeated the run with stepwise increases and decreases in peripheral resistance. Having done that we tried to restore cardiac function by increasing left atrial filling pressure. We did this by trying to duplicate the control condition, which we had obtained at the start of the experiment, with respect to the values of mean aortic pressure and peripheral resistance. This new level of left atrial filling pressure varied between 8 and 12 cm H2O (n = 10). After this compensation we executed stepwise increases and decreases of the peripheral resistance for the third time. The complete experiment was performed within 45 minutes. We report here on 10 successful experiments on 10 different hearts.

Results

To give some insight into the functional state of the isolated heart preparation, an example of the variables recorded during a control situation is presented in Figure 3 in combination with similar records from a cat with open thorax.

Relevant data from each experiment are given in Figure 4. We plotted here the relationship between mean left ventricular pressure and mean aortic flow for each setting of the peripheral resistance in the three experimental situations. Linear regression analysis was performed on each set of points obtained during each experimental situation for each heart. Results of this analysis are given in Table 1. In this table the pumping capacity of the heart is described by its source resistance (the slope of the lines in Figure 4) and the mean hydromotive pressure, given by the intercept of the lines with the vertical axis. The table also includes the

![Figure 4](http://circres.ahajournals.org/). Graphic presentation of the experimental results for 10 experiments on isolated cat hearts. Measurements made during the control situation are represented by O and ‡, measurements after infarction by ▽ and ♦, and measurements after compensation by Δ and ▲. Mean left ventricular pressure is given in mm Hg, mean aortic flow in cm3/sec. Data represented by open symbols were obtained when peripheral resistance was increased, and the solid symbols represent data obtained when peripheral resistance was decreased.
correlation coefficients for the lines, the peripheral resistances for the control settings, and heart rates.

When we compared the condition after infarction with control we found a significant decrease in mean hydromotive pressure. Source resistance did not change significantly after infarction. After the infarct cardiac output was restored to the control level by an increase in left atrial filling pressure and thus by the Frank-Starling mechanism. In this situation mean hydromotive pressure was not significantly different from that found during control conditions. Eight of the 10 hearts showed a lower source resistance after compensation in comparison to the control value; in two hearts the opposite was true. We could not demonstrate a statistically significant change in source resistance between these two situations at the 5% level.

To summarize our findings for the 10 experiments we determined mean values for the three experimental situations and plotted the results in Figure 5.

In the experiments described above, left atrial filling pressure was kept constant by an overflow system. This is not precisely the same as keeping left ventricular end-diastolic pressure or volume constant. With increasing aortic pressure we found a slight increase in left ventricular end-diastolic pressure in spite of the fact that left ventricular filling time decreases with an increase in aortic pressure. This is demonstrated in Figures 6 and 7. Figure 6 shows left ventricular end-diastolic pressure plotted as a function of the end-diastolic pressure in the aorta. The points in this graph were obtained from the control runs of nine experiments. Figure 7 shows two left ventricular pressure tracings obtained in a control run for two situations in which aortic pressures differed. The widening of the left ventricular pressure pulse with the increase in ventricular load and the consequent shortening of left ventricular filling time are illustrated.

**Discussion**

The concept of source impedance of the heart is particularly suitable for quantification of the pumping ability of the heart and has the advantage of being a quantity purely

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**TABLE 1**  
Heart Rates (HR), Peripheral Resistances (R_p), Source Resistances (R_s), and Mean Hydromotive Pressures (HMP) of “Control” Runs, “Infarct” Runs, and “Compensated” Runs per Heart

<table>
<thead>
<tr>
<th>Expt no.</th>
<th>HR (beats/min)</th>
<th>R_p (mm Hg/cm sec)</th>
<th>HMP (mm Hg)</th>
<th>r</th>
<th>R_s (mm Hg/cm sec)</th>
<th>HMP (mm Hg)</th>
<th>r</th>
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<td>Control</td>
<td>Infarct</td>
<td>Compensated</td>
<td></td>
<td></td>
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<td>72.1 ± 8.4</td>
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<td>9.2 ± 3.4</td>
<td>79.4 ± 8.4</td>
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<tr>
<td>130375b</td>
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<td>8.9 ± 3.4</td>
<td>78.9 ± 16.8</td>
<td>33.5 ± 4.6</td>
<td>9.1 ± 3.4</td>
<td>74.5 ± 8.4</td>
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</table>

* Peripheral and source resistance are given in terms of 10^4 g cm^-2 sec^-1; 10 g cm^-2 sec^-1 ~ 10^-6 kg m^-4 sec^-1. Values for peripheral resistance are those measured for the starting situation for each run.

† 10 mm Hg ~ 1.33 kPa. Only the mean hydromotive pressures obtained from the “infarct” and “control” situation are significantly different at the 5% level (Wilcoxon matched pairs signed ranks test).

r = correlation coefficient of the linear regression analysis used to obtain R_s and HMP.
dependent on cardiac function, and not directly influenced by changes in the peripheral system. This contrasts with, for instance, ventricular function curves. Both source impedance and ventricular function curves try to describe a particular aspect of cardiac function, but the shape of the ventricular function curve is dependent on the "setting" of the loading system and, therefore, it is not a specific cardiac quantity. This dependency on the load is demonstrated by two ventricular function curves obtained from an experiment on the isolated cat heart and shown in Figure 8. Here cardiac output is plotted as a function of left ventricular end-diastolic pressure under two different experimental conditions. In one situation mean aortic pressure was kept constant by changing peripheral resistance, while in the other peripheral resistance remained unchanged. Relating stroke work to left ventricular end-diastolic pressure does not change this dependency essentially, because stroke work also is a function of the peripheral resistance.

Tying off a part of a coronary artery resulted in a decrease in cardiac output. Analysis of the data showed that this was due to a change in hydromotive pressure and that source resistance remained unaffected. When cardiac output was restored to control value by increasing atrial filling pressure, we could demonstrate no statistically significant difference in source resistance and hydromotive pressure between the control and compensated situations. This means that the volume of blood the heart could pump per unit of time against different loads in the control situation was not diminished after infarction and subsequent compensation. Thus we could not tell from the hydromotive pressure or the source resistance whether the heart was damaged or not when these two situations were compared. This demonstrates how effectively an increase in filling pressure compensates for a certain loss of active muscle in the ventricular wall.

One must of course bear in mind that 8 of the 10 hearts showed a decrease in source resistance after compensation as compared to control values, and the possibility that a larger series would show a significant decrease of this value cannot be excluded. However, it appears not to be a consistent finding for all hearts.

We showed that an increase in aortic pressure was related to a slight increase in left ventricular end-diastolic pressure in spite of a constant left atrial filling pressure and a decrease in ventricular filling time. This change in left ventricular end-diastolic pressure could be due to a change in the left ventricular end-diastolic pressure-volume relationship which, in turn, was caused by an increased perfusion pressure in the coronary arteries. If this is true, left ventricular end-diastolic pressure cannot be used as an index of left ventricular end-diastolic volume in these experiments and it is then very difficult to estimate the possible change in left ventricular end-diastolic volume with a change in aortic pressure without measuring the former variable.

Our experiments were designed in such a way that points in the plot of mean left ventricular pressure against mean aortic flow were obtained by first increasing and then decreasing the peripheral resistance of the load. Points obtained by increasing resistance fell on the same line as points obtained by decreasing ventricular load. This demonstrates the stability of the preparation and the reproducibility of the measurements.

Considering a model like that presented in Figure 1, one assumes the hydromotive pressure to be constant and the source resistance to be constant and linear. If the points in
the plot of source resistance fall precisely on a straight line, these assumptions are likely to be true. The values of the correlation coefficients presented in Table 1 do suggest that in most cases a straight line fits the data well. However, the degree of linearity seems to vary between hearts. Sometimes a slightly curved line seems to fit the results better than a straight line. Two extreme examples, measured for two different hearts, are shown in Figure 9. When a more curved relationship is found it is always in the direction shown in Figure 9. This sort of curvature is in agreement with the observation of Bergel (discussion of Elzinga and Westerhof) that the predicted mean hydromotive pressure obtained by extrapolation is greater than the measured mean hydromotive pressure determined from an isolomitive beat. The cause of this is not yet clear to us. However, in a physiological working range (mean left ventricular pressure of 50–70 mm Hg and mean aortic flow of 2–5 cm³/sec) a linear approach seems to be reasonable.

In conclusion we would like to state that the source impedance concept appears to be a useful tool to describe the pumping ability of the heart in quantitative terms. Occlusion of a part of the coronary arterial system affects the hydromotive pressure but not the source resistance. The pumping ability of the left heart can, after infarction, be restored almost completely by an increase in left atrial filling pressure. The Frank-Starling mechanism which the heart can use to compensate for the effects of a loss in contractile tissue therefore seems to be very effective in this situation.

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We thank I.T. Gabe, C.J. Mills, and M.I.M. Noble for the stimulating discussions on the concept of source impedance.

References


Electrophysiological and Antiarrhythmic Effects of Propranolol in Canine Acute Myocardial Ischemia

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SUMMARY To correlate the antiarrhythmic and electrophysiological effects of propranolol in acute myocardial ischemia, we examined the effects of temporary (15-minute) ligations of the left anterior descending coronary artery in studies on 15 dogs. We recorded bipolar electrograms and monophasic action potentials from the ischemic and normal zones and measured the intervals from the onset of QRS in a standard electrocardiogram lead to the major deflection of electrograms recorded from the ischemic and normal zones. We also determined monophasic action potential duration (APD) and effective refractory period (ERP). Data for control ligations were compared to those during which propranolol, 40 μg/kg, was administered intravenously immediately after ligation. Propranolol reduced the mean number of ventricular beats per minute (from 15 to 6) (P < 0.01). Propranolol slowed conduction in the ischemic zone (by 10 msec at peak effect, P < 0.01) and had no or only a very slight effect (by 1-msec at 15 minutes, P < 0.05) on conduction in the normal zone. Propranolol also prolonged APD in the ischemic (32-msec) and normal (14-msec) zones (P < 0.01), prolonged ERP in the ischemic (41-msec) and normal (20-msec) zones (P < 0.01), and reduced the APD/ERP ratio in the ischemic (1.62 to 1.47) (P < 0.01) and normal (1.62 to 1.55) (P < 0.05) zones. During the control ligation, APD in the ischemic zone was 25 msec shorter than in the normal zone (P < 0.01), but with propranolol the difference was not significant. The effects of propranolol in slowing conduction in the ischemic zone, in prolonging refractoriness, in reducing APD/ERP, and in reducing the disparity in APD between ischemic and normal zones may explain its demonstrated antiarrhythmic effects in acute myocardial ischemia.

SPECULATION on the mechanism of action of antiarrhythmic drugs is based in large measure on microelectrode studies of normal, isolated cardiac tissue. In these studies, the effects of an agent on various parameters including conduction, action potential duration, and refractory period are determined and the results are extrapolated to the arrhythmic, abnormal heart in situ. However, there are limitations to this method because the effects of antiarrhythmic drugs on the electrophysiological properties of normal

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