Combined effects of aortic and right atrial pressures on aortic flow

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HERNDON, CALEB W., AND KIICHI SAGAWA. Combined effects of aortic and right atrial pressures on aortic flow. Am. J. Physiol. 217(1): 65-72. 1969.—Aortic flow (AF = cardiac output minus coronary flow) was determined as a function simultaneously of both mean aortic pressure (MAP) and mean right atrial pressure (MRAP). In 10 dogs MAP was altered from 30 to 300 mm Hg while keeping mean right atrial pressure (MRAP) at fixed levels. In another 11 dogs MRAP was increased from 0 to 20 mm Hg, while keeping MAP at specified levels. When MRAP was within the physiological range, the heart-lung compartment could pump an almost constant AF until MAP rose above 180 mm Hg. However, left atrial pressure rose even though right atrial pressure did not. AF decreased abruptly toward zero as the MAP approached 254 mm Hg (MAP max). When the arterial baroreceptor reflex was intact, MAP max was attenuated approximately 25%. Such a comprehensive analysis in which the full range of flow responses of the pump (heart-lung compartment) to MAP and MRAP alterations provides necessary data for use in systems analyses of the circulation.

SINCE THE TIME OF Frank and Starling, investigators have been interested in the variables controlling cardiac function, and yet the significance of one of these, aortic pressure, still remains controversial both qualitatively and quantitatively. From a qualitative standpoint, many physiologists have assumed that aortic pressure affects cardiac output in a major way without thoroughly investigating the problem (12, 15, 18, 26, 29). However, others have seen cardiac output remain relatively normal in the face of elevated aortic pressures and have, therefore, minimized this influence of aortic pressure (4, 10, 19). Sarnoff et al. (22) derived valuable data on the effect that changes in aortic pressure and right atrial pressures on aortic flow (cardiac output minus coronary flow) alone, and 2) the interrelated effects of input and output pressures on aortic flow (cardiac output minus coronary flow) in controlled experiments over wide ranges heretofore neglected in studies on the heart-lung compartment.

METHODS

This study was carried out in 25 dogs divided into three series of experiments. The dogs weighed between 10 and 15 kg and were anesthetized with morphine sulfate (2 mg/kg) and a-chloralose (80 mg/kg).

Figure 1 illustrates the basic preparation. The goal of this preparation was to allow simultaneous and exact control of mean aortic pressure and mean right atrial pressure.

The chest was opened via a midsternal incision. Respiration was maintained with intermittent positive-pressure ventilation. The left subclavian artery was sectioned and cannulated. One cannula was directed distally and served as part of the systemic perfusion system, while another cannula was directed proximally and served to record aortic arch pressure (mean aortic pressure (MAP)). The distal end of the aortic arch was cannulated with a 10-mm inner diameter glass cannula. Blood pumped by the left heart flowed through this cannula into an external circuit of rubber tubing which passed through a servo-controlled artificial resistance regulator. From this resistance regulator, the blood was directed through a rotameter for aortic flow measurements, after which it emptied into a heated reservoir. From this reservoir, blood was infused by a variable speed Sigma motor pump back into the descending aorta.
FIG. 1. A schematic illustration of surgical procedure, experimental apparatus, and recording system. Right and left are abbreviated R and L. P represents pressure. For detailed explanations, see text.

FIG. 2. Part of an experimental recording of series I experiment in which mean right atrial pressure (MRAP) was fixed at 8 mm Hg and mean aortic pressure (MAP) was varied stepwise from 30 to 270 mm Hg to study its effect on aortic flow (AF). Note absence of significant changes in mean left atrial pressure until MAP was elevated beyond 180 mm Hg.

and left and right subclavian arteries. The right subclavian cannulation was directed toward the heart so that during descending aortic cannulations it could bypass part of the blood dammed in the aortic arch through a cannulated femoral artery into the abdominal region. This moderated the severity of abdominal ischemia associated with the aortic cannulations. It also helped to moderate excessive rise in MAP during aortic cannulations. When all other vessel cannulations were completed, the brachiocephalic artery was tied off, rendering the aortic arch blind except for the outflow channel through the resistance regulator.

The right atrial appendage was cannulated with a 10-mm inner diameter glass cannula through which a variable amount of blood was shunted to the heated reservoir positioned below the level of the dog’s heart. The amount of this shunt flow was automatically adjusted by another servo-controlled resistance regulator so that mean right atrial pressure (MRAP) could be maintained at the desired level regardless of changes in aortic flow (AF) or systemic venous return. By virtue of these two sets of servomechanisms, both MAP and MRAP could be controlled at any desired level within ± 2.5 mm Hg for MAP and ± 0.4 mm Hg for MRAP.

Bilateral vagotomy was performed in series I and II to eliminate ventricular and aortic baro- and chemoreceptor reflex intervention on cardiac performance. After vagotomy, heart rate became remarkably constant (Fig. 9 or ref 13). The carotid sinus nerves were ligated bilaterally to prevent...
All vertebral artery originated from the right subclavian artery. The right subclavian artery was ligated at a site distal to the brachiocephalic, but proximal to the point where the right common carotid artery left that artery. The external carotid and vertebral arteries were cannulated and perfused by the perfusion pump at a constant pressure to maintain the circulation to the head. First, AF was monitored as MAP was elevated from 30 mm Hg to MAP max (typical series I procedure) while the heart was under the influence of the reflexes from both receptor regions. Then, the carotid sinus nerves were ligated very tightly leaving only the aortic receptors to influence the system as MAP was again elevated from 30 mm Hg. Finally, the vagi were cut leaving the preparation to respond to similar elevations of MAP without any reflex intervention from these receptors. Heart rate was monitored with a Grass tachograph model 7P-4A.

The difference in experimental procedure between series I and II will be explained in the presentation of results.

RESULTS

Series I: effect of MAP elevation on AF at various levels of constant MRAP. The influence of MAP on AF was examined by elevating MAP stepwise from 30 to nearly 300 mm Hg while recording the changes in AF in 10 preparations. This examination was made with the initial AF set at three different levels (100, 150, and 200 ml/min per kg body wt) in each preparation. To attain the desired initial flow level, MRAP was adjusted to a low, medium, or high level (0–4, 4–6, or 6–8 mm Hg) while MAP was maintained near 50 mm Hg. Following this initial adjustment, MRAP was held constant thereafter by the servomechanism. Then, MAP was further lowered to 30 mm Hg for a short period of time (30 sec) and thereafter elevated in steps of 30 mm Hg until AF became unmeasurably small. The maximum MAP that individual preparations developed will be symbolized by MAP max.

After each step elevation in MAP, AF responded with a brief undershoot and then stabilized at a new AF level within 10–15 beats. The interval between successive elevations of MAP was 2 min or less; data were taken only after AF had stabilized for 30 sec or more. Figure 2 is a typical experimental recording of the influence that elevations of MAP from 30 to 270 mm Hg exerted on AF while MRAP was held at 8 mm Hg. The AF level initially established was usually maintained by the heart until MAP was elevated above 180 mm Hg, beyond which AF fell toward zero as MAP approached a MAP max of around 250 mm Hg. The relationship between AF and MAP was similar for all flow levels investigated; the MAP above which AF began to fall significantly seemed to be influenced only slightly by the flow level or MRAP level. Heart rate remained almost exactly constant regardless of MAP. Accordingly, the fall of AF following elevations of MAP was caused by diminution of stroke volume. In about one-half of the preparations, the MAP-AF relationship was first determined at the high flow level (200 ml/min per kg body wt), followed by the middle one (150 ml/min per kg body wt), and then the lowest (100 ml/min per kg body wt). In the other half, the sequence was reversed. No significant difference between the two sets of results could be detected.

To summarize the results, AF was normalized on basis of weight to give nAF, and MAP was normalized to give sinus receptors together with the aortic arch receptors to be exposed to the pressure in the carotidocarotid blind sac. The external carotid and vertebral arteries were cannulated and perfused by the perfusion pump at a constant pressure to maintain the circulation to the head. First, AF was monitored as MAP was elevated from 30 mm Hg to MAP max (typical series I procedure) while the heart was under the influence of the reflexes from both receptor regions. Then, the carotid sinus nerves were ligated very tightly leaving only the aortic receptors to influence the system as MAP was again elevated from 30 mm Hg. Finally, the vagi were cut leaving the preparation to respond to similar elevations of MAP without any reflex intervention from these receptors. Heart rate was monitored with a Grass tachograph model 7P-4A.

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nMAP as percent of the MAP\textsubscript{max} determined in the same run. For example, an MAP value of 30 mm Hg would correspond to 10% if the MAP\textsubscript{max} was 300 mm Hg in the same run. The average, normalized results are shown in Fig. 3, showing MAP-AF relationships at three different flow levels. Also, the mean values for MAP\textsubscript{max} in mm Hg are shown in Fig. 3. Between MAP\textsubscript{max} (maximum mean aortic pressure attained with infinite resistance to aortic flow) and each of the three initial levels of AF there was found to be no statistically significant correlation. On this basis, the mean and standard deviation of all the measured values of MAP\textsubscript{max} was calculated to be 254 ± 23 mm Hg.

With MAP at levels of 60, 120, 180, and 240 mm Hg, measurements of mean left atrial pressure (MLAP) and mean pulmonary arterial pressure (MPAP) made simultaneously in these studies were recorded and are shown in Fig. 4. These are averaged values of resulting pressures for all flow levels investigated. Notice the constancy of the pressures until MAP was elevated beyond 180 mm Hg.

**Series II:** Effect of MRAP elevation on AF at constant MAP.

In a separate group of 11 dogs, AF was determined at various specified MAP levels while elevating MRAP stepwise. This series of experiments was essentially equivalent to the series I experiments, except that the primary independent variable and the fixed parametric variable were exchanged between the two runs.

Figure 5 illustrates an experimental record from a typical series II run which usually lasted from 4 to 7 min. Figure 6 is a plot from a complete recording, which shows the response of AF to MRAP elevations at several MAP levels. The MRAP-AF curves at relatively low MAP levels (50–150 mm Hg) were almost linear and were largely superimposed on each other over a wide flow range. This was confirmed in all experiments studied. Furthermore, no significant difference was observed among their AF plateau levels. As MAP was further increased to 180 and then to 200 mm Hg, the curves began to deviate with increasingly less steepness and lower plateau levels.

From the series II experiments in which the MRAP-AF curves were determined at MAPs of 50–180 mm Hg, the mean slope (ΔnAF/ΔMRAP) was found to be 52.2 ± 17.1 ml/min per kg body wt per mm Hg (Fig. 7). The intercepts of these curves extrapolated to the MRAP axis averaged 1.9 ± 1.7 mm Hg. The mean AF plateau level was 365.8 ± 88.9 ml/min per kg body wt.

**Series III:** Baroreceptor influence on relationship between MAP, MRAP, and AF.

In series III, four successful preparations were used to characterize the influence of the baro- and chemoreceptor reflexes on the MAP-AF relationship. Figure 8 illustrates the MAP-AF relationship with and without the influence of the reflexes in one dog. The short-dash curves connecting the crosses represent the MAP-AF relationship at three AF levels under both carotid and aortic reflex control. The solid line curves connecting the closed circles were determined after the carotid sinus nerves had been tightly ligated and effectively denervated bilaterally. The long-dash curves connecting the open circles were determined after bilateral vagotomy. Note the progressive extension of the curves toward higher MAP levels as the reflex inhibition was progressively removed. Figure 9 shows the heart rate response to MAP elevations recorded simul-
AORTIC FLOW VS. AORTIC AND RIGHT ATRIAL PRESSURES

DOG: 15.3 Kg

AORTIC PRESSURE
100; 150 mm/Hg
50 mm/Hg
180 mm/Hg
200 mm/Hg

RIGHT ATRIAL PRESSURE (mm Hg)

FIG. 6. An example of plots obtained in series II experiments on a 15.3-kg dog. Mean aortic pressure (MAP) was fixed at 50, 100, 150, 180, and 200 mm Hg. At each specified MAP, mean right atrial pressure (MRAP) was varied from 0 to 20 mm Hg to determine aortic flow (AF) which was normalized in terms of ml/min per kg body wt.

Simultaneously with the data shown in Fig. 8, values for heart rate were taken 30 sec following each MAP elevation.

When MAP was initially lowered from the resting level of 100 to 60 mm Hg at outset of these experiments, a decrease in heart rate was consistently noticed only when the baroreceptors were intact. Green (8) explains this as the distortion of the collapsing arterial wall causing the baroreceptors to fire. The heart rate returned toward the resting level as MAP was elevated toward its resting level. Then heart rate decreased as MAP was elevated beyond 100 mm Hg as expected (13).

All the MAPmax values obtained in series III experiments were grouped with respect to the reflex control status. For all of the MAPmax values derived with intact carotid and aortic reflexes, the mean was 194.4 ± 21.4 so mm Hg. It rose to 220.3 ± 26.2 mm Hg when the carotid reflexes were bilaterally removed. Following bilateral vagotomy, the mean MAPmax reached 261.8 ± 26.5 mm Hg. All the differences among these mean values were statistically significant (P < 0.005).

DISCUSSION

Comparison of pressure-load characteristics of heart-lung compartment vs. isolated left ventricle. The most important observa-

tion of these studies was the extremely high aortic pressures against which the heart can pump without altering its output, even though the right atrial pressure remains exactly constant. This effect is not observed when one studies the relationship between left ventricular output and left atrial pressure.

The left ventricular mean aortic pressure-aortic flow (MAP-AF) curves determined in a previous study (20) while maintaining mean left atrial pressure at different levels showed progressively increasing dependence of AF on MAP as the left atrial pressure was raised. Comparable curves from the present studies (Fig. 3) extended almost horizontally to MAP values of 180 to 200 mm Hg, after which AF fell more rapidly than seen in the case of the left ventricular curves. This difference between the two studies probably resulted from the fact that the Starling mechanism was still operative in the left ventricle of the present study.
since left atrial pressure was allowed to vary. For example, when MAP was elevated in the higher pressure ranges, a resulting temporary decrease in AF allowed the blood volume of the left heart to increase. This was reflected by a rise in MLAP, and it allowed the Starling mechanism to increase AF back to normal. This mechanism would allow the left heart to maintain AF up to higher MAP levels than would be true if the mechanism were inhibited by keeping MLAP constant as in the former study (20). If MAP were suddenly raised by constricting the aorta in animals with natural circulations, such blood volume shifts would take place during the initial 2-3 sec after the constriction. The reasons are that 1) systemic venous pressure would not fall to any significant degree during the first few seconds following the sudden decrease of arterial inflow into the systemic vascular bed, because of the high compliance of the venous capacitance vessels; and consequently, 2) the right heart would be able to pump more than the left heart was pumping during this period with some amount of blood being dammed in the heart-lung compartment. After a few seconds, however, decreased systemic venous return would ensue and lower the input pressure (right atrial pressure) of the heart-lung compartment. On the other hand, homeometric autoregulation would develop in the left ventricle by this time and would cooperatively work with the Starling mechanism (from the elevated left atrial pressure) to augment left cardiac outflow toward the control level. This, in turn, would bring the reduced systemic venous return toward its control level. Thus, a new equilibrium state would result among a set of hemodynamic variables such as right atrial pressure, right ventricular outflow, left atrial pressure, left ventricular outflow, and systemic venous return. The blood volume shifts which can be estimated from the pressure changes shown in Fig. 4 (multiplied by compliance values found in the literature (1)) reveal an important parametric requirement that the heart-lung compartment places on the systemic vascular system. Fulfillment of this requirement by the systemic vascular bed enables the heart to maintain a relatively constant AF under the equilibrated levels of MRAP and MAP; this supplements that which the left ventricle can pump by virtue of the homeometric autoregulatory mechanism alone.

The rise in mean left atrial pressure that occurred in the present study as mean aortic pressure was increased to 180 mm Hg was never greater than 2 mm Hg. This was not enough rise to cause a measurable back-loading effect on the right ventricle. Therefore, the right ventricle continued to pump at the same output rate (and the left ventricle also) despite the rising aortic pressure. One factor that theoretically prevents back loading of the right ventricle when the left atrial pressure rises only a few millimeters Hg is the pulmonary vascular waterfall effect; that is, until the left atrial pressure rises above the waterfall pressure in the pulmonary capillaries it cannot cause a rise in pulmonary arterial pressure. Indeed, measurements of pulmonary arterial pressure showed that it did not rise significantly until the aortic pressure was elevated beyond 180 mm Hg, which was also the level at which aortic flow began to decrease.

Composite three-dimensional relationships between MRAP, MAP, and AF. One of the major reasons for undertaking this project was to obtain data for use in systems analyses of the circulation. The data used previously has been scanty, has had a narrow range, and has not considered both right
atrial pressure and aortic pressure effects on heart action simultaneously. Figure 10 gives the mean values derived from this study in three-dimensional form, considering simultaneous interrelationships for complete physiological ranges between the three factors: 1) mean right atrial pressure, 2) mean aortic pressure, and 3) aortic flow.

Another principal objective of this study was to derive the most quantitatively accurate results possible for aortic flows; therefore, considerable attention was given to preparing experiments of the highest quality. The mean value of MAP_max (254 mm Hg), together with MAP_max values of 280–300 mm Hg (at mean left atrial pressures of 10–15 mm Hg) in some preparations, indicated a high degree of validity of our preparations, for these pressure levels even exceeded some of the peak systolic left ventricular pressures (PSLVP) reported in the literature for the isovolumically contracting left ventricle of the dog. For example, Monroe and French (18) reported PSLVP of 125 mm Hg with a left ventricular end diastolic pressure (LVEDP) of 45 mm Hg. Ullrich et al. (27) obtained a PSLVP of about 300 mm Hg with LVEDP at about 15 mm Hg in one experiment. Taylor et al. (25) determined PSLVP values of 152–338 mm Hg at LVEDP values of 3.4–12.3 mm Hg.

In addition, the AF plateau level of 365.8 ml/min per kg body wt and the slope of 52.2 ml/min per kg body wt per mm Hg determined in the series II experiments compare favorably with a similar curve derived by Bishop et al. (2) in conscious intact dogs which had an AF plateau level of 340 ml/min per kg body wt and a slope of 45 ml/min per kg body wt per mm Hg.

Baroreceptor influence on AF-MAP-MRAP relationship. In series III the influence of the baroreceptor reflexes on the MAP-AF curve and on heart rate was studied. The inhibitory effect of the reflex was manifest by remarkable decreases in MAP_max values. This change probably resulted from two mechanisms: 1) a negative inotropic effect of the reflexes on the heart, 2) a negative chronotropic effect on heart rate. This finding is in keeping with the well-documented findings that the carotid sinus reflex suppresses the peak systolic pressure developed by the left ventricle (16). It is also in consonance with Scher’s (23) finding based on a statistical factor analysis that both MAP and heart rate play an important role in determining left ventricular stroke volume in dogs with intact baroreceptor reflexes.

The present findings indicate that the overall influence of the baroreceptor reflex on the heart-lung compartment can be illustrated in terms of the shift of the MAP-AF curves toward a lower mean aortic pressure (MAP) range.

It is worthwhile to consider here another effect of the baroreceptor reflexes on the systemic capacitance vessels which indirectly influences the pumping capacity of the heart-lung compartment within the natural circulatory loop system. Glick and Yu (7), Braunwald et al. (3), and many others amply proved that systemic venous capacitance increases via these reflexes when MAP rises. This is a factor which tends to reduce the blood volume shift from the systemic vascular bed into the heart-lung compartment. Consequently, the capacity of the heart-lung compartment to maintain a prescribed AF during MAP elevation would diminish after the ensuing venous pooling. A consideration of this additional aspect of the reflex action leads one to the prediction that impeding AF distal to the baroreceptor sites in animals with intact reflexes would reduce AF by an amount more than expected from the MAP-AF curves in Fig. 8. In addition, the increase of venous capacitance and decrease of arterial resistance caused by these reflexes appear to take effect at a relatively lower MAP range than that for the effect on cardiac contractility or heart rate (17, 24). The effect on AF of such unloading at the input site of the heart-lung compartment by increasing venous capacitance is directionally opposite to the simultaneous unloading effect of the reflex on AF at the output site of the heart-lung compartment by decreasing arterial resistance. The quantitative differentiation of the reflex effects on the arterial resistance, venous capacitance, and cardiac pump cannot be made from documents obtained in the natural circulation unless one has data on 1) the input and output pressure characteristics of the heart-lung compartment (such as presented in the present study) and on 2) the basic impedance characteristics of the systemic vascular compartment, including the behavior of the capacitance vessels with and without the reflex intervention.

In conclusion, it should be emphasized that variations of mean aortic pressure up to 180 mm Hg were found to exert a negligible effect on the steady-state aortic flow from the heart-lung compartment when the right atrial pressure was controlled constant. This effect has not been seen in studies in which the left ventricular end-diastolic pressure or the left atrial pressure has been held constant. This emphasizes the importance of studying the entire heart-lung compartment, as well as individual parts of the heart, when one is interested in the role of the heart in the entire circulation.

This study was supported by Public Health Service Research Grant HE-10581.

C. W. Herndon was supported by National Institutes of Health Training Grant 5T1-GM-316.

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Received for publication 6 November 1968.

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