Flow patterns in cavae, pulmonary artery, pulmonary vein, and aorta in intact dogs

BEVERLY C. MORGAN, FRANCIS L. ABEL, GAY L. MULLINS, AND WARREN G. GUNTHEROTH
Division of Pediatric Cardiology, University of Washington
School of Medicine, Seattle, Washington

FLOW PATTERNS in the aorta and pulmonary artery have been described in relation to one another by Franklin, Van Citters, and Rushmer (5), but the precise relationship of these two flow patterns to respiration remains uncertain in the intact animal. Flow records from the vena cavae, including clear demonstration of the pumping effect of inspiration, have been published by Brecher and Hubay (2), although these were from acute animal experiments. Flow patterns have been briefly reported in the pulmonary veins (8), but the relationships of these patterns to inspiration or to flow in the great vessels have not been demonstrated.

Several physiological and pathophysiological phenomena depend on the relationships of flows in the venous tributaries to variations in stroke volume in the right and left ventricle, and on the effects of respiration on these flows. Although right ventricular systole is reported (2) to accelerate flow into the right atrium (via a fronte), the only report (8) of flow patterns in the pulmonary veins attributes the forward flow to a transmitted pulse from the pulmonary artery (via a tergo). Inspiration is said to cause an increase in vena caval flow (2) and to cause a reduction in pulmonary venous return by producing pooling of blood in the pulmonary veins (6).

In conflict, however, is the report that the right and left ventricular stroke volumes are covariant, at least within one or two beats (5).

We have recorded simultaneous flow patterns in awake animals from the vena cava, pulmonary artery, pulmonary vein, and aorta. The pulsatile flow patterns of the veins were studied in relation to both the cardiac and respiratory cycles, and the variations in stroke volume of the ventricles were correlated with each other, with filling interval, and with respiration.

MATERIALS AND METHODS

Forty dogs, weighing 17-30 kg, were subjected to thoracotomy. Ultrasonic flow transducers (4, 9) were implanted at the base of the aorta and pulmonary artery, on the superior or inferior vena cava near the right atrial junction, and on a left lobar pulmonary vein immediately outside the pericardium. A flat Silastic balloon, 20 x 25 mm, was placed in the pleural space. The animal was then allowed to recover. Data were recorded 5 days to 6 weeks postoperatively. Records were obtained while the animal was awake, although more frequently data were recorded under light general anesthesia (morphine, 1-1.5 mg/kg, and pentobarbital, 10-15 mg/kg). Arterial, venous, and intracardiac pressures were measured by catheterizing appropriate vessels or chambers. Pressures were recorded by means of

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2 Present address: Dept. of Physiology, Indiana University School of Medicine, Indianapolis, Ind.
Statham P23Db (arterial), P23BB (venous), and Sanborn 276 (pleural) transducers with zero level at the estimated mid-right atrium. All animals appeared to be in excellent health at the time of study. It was not possible to record all of the variables in every animal because of failure of some components during the course of the recovery.

The flow records were not ordinarily calibrated, since interest was in relative changes from beat to beat and in alterations produced by respiration. Zero level for venous flows was determined by intravenous administration of acetylcholine in dosages sufficient to produce transient cardiac arrest (2–4 mg). Relative stroke volume was estimated by planimetry of the systolic flow pulse. Statistical analyses were performed on an IBM 7094 on data from some of the animals with complete records.

RESULTS

Effects of heart beat: venous flow. Vena caval flow records in our intact, awake animals were similar to records obtained by Brecher using a bristle flowmeter in acute experiments (2). There was regularly a brief reversal of flow with atrial systole (Figs. 1, 2), considerably enhanced by longer diastolic intervals. There were two major forward-flow waves with each cardiac cycle, one during ventricular systole, and a second peak in ventricular diastole. The relative magnitudes of these waves were variable, but the systolic pulse was usually greater. The onset of the first positive wave in the vena cava was nearly simultaneous with the onset of aortic ejection, with a maximum delay of .05 sec. There was frequently no plateau after the regurgitant flow of atrial systole, so that the upstroke was continuous from the nadir of the regurgitant pulse to the peak of the forward-flow pulse. (That these were separate pulse phenomena, however, was evident with tachycardia, during which the regurgitant pulse tended to disappear.) The peak of the diastolic flow pulse was quite varied in its timing, but its onset was within .06 sec of the end of aortic ejection. A third, relatively low-amplitude flow pulse occurred later in diastole, but was not always present.

Pulmonary venous flow records were remarkably similar to vena caval flow in their temporal relationship to the cardiac cycle (Fig. 1). Left atrial contraction produced a brief retrograde pulse which became more prominent with longer diastolic filling periods. The onset of left ventricular systole was accompanied by increased flow in the pulmonary vein; a second increase in flow, which often exceeded the systolic pulse, occurred during ventricular diastole. A third, minor flow pulse was sometimes seen in late diastole. The only regularly present positive pressure pulse of magnitude in the pulmonary vein was coincident with atrial systole (Fig. 3).

Pulmonic and aortic flow patterns. Ejection from the right ventricle usually preceded ejection from the left ventricle.
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FIG. 3. Record of four flows in relation to intrathoracic pressure and pulmonary vein pressure. Note that the only major pressure change in the pulmonary vein is accompanied by a retrograde-flow pulse.

Effects of respiration. Pressure changes in the right atrium, intrathoracic venae cavae, and pulmonary vein followed changes in intrathoracic pressure relatively closely (7). Pressure in the abdominal vena cava was less affected by inspiration and frequently showed a small increase of 1-2 mm Hg with inspiration; intrathoracic caval pressure uniformly showed a decrease of 1-5 mm Hg with inspiration. Pressure in the right ventricle and pulmonary artery consistently showed a small but definite decrease with inspiration, whereas net (transmural) pressure increased slightly. Inspiration generally decreased the systemic systolic pressure, whereas the diastolic pressure increased uniformly, resulting in a narrowed pulse pressure. Inspiration also increased the heart rate promptly (Table 1).

The respiratory cycle significantly affected the magnitude of flow in all vessels. However, the effect of respiration was dependent to a large degree on the depth and frequency of respiration and on the heart rate: slower respiratory or cardiac rates were generally associated with more marked changes. In the presence of either tachypnea or tachycardia, variations in stroke volume decreased. The most pronounced changes occurred with sinus arrhythmia.

Vena caval flow pattern showed an increase within the time of one heartbeat of the onset of inspiration. Peak vena caval flow was attained rapidly with inspiration, usually at the nadir of intrathoracic pressure (Fig. 2).

Right ventricular stroke volume was augmented by inspiration in one-half the instances (Table 1), generally within one or two beats following the onset of inspiration (Fig. 2), and within one beat of the increase in vena caval flow. The total pulmonary blood flow almost always increased during inspiration, since the heart rate usually increased and the pulmonary flow is the product of the rate and stroke volume. The variance in stroke volume even with sinus arrhythmia was not great; standard deviations varied from 4 to 17% of the mean. With tachycardia, there was no significant variation in either filling interval or stroke volume.

Pulmonary vein flow also was significantly modified by respiration. Occasionally a diphasic pattern occurred with inspiration, an early increase in flow followed by a decrease, but the usual pattern with inspiration was a...
Table 1. Effect of inspiration on stroke volume (SV) and flow (SV × rate)

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Rate</th>
<th>Pulmonary Artery</th>
<th>Aorta</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SV</td>
<td>SV × rate</td>
</tr>
<tr>
<td>9</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>16</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>34a</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>34b</td>
<td>o (Tachycardia)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>32</td>
<td>o (Tachycardia)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>38</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>20</td>
<td>o (No SA)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>39</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
</tbody>
</table>

Summary:
- Increase: 6
- Decrease: 2
- No change: 3

Net changes with inspiration in rate, stroke volume, and stroke volume × rate for the right and left ventricles. SA indicates sinus arrhythmia. Note that although the aortic stroke volume generally declined with inspiration, the rate accelerated and the total aortic flow with inspiration increased in 5 of 9 animals.

significant increase in pulmonary venous return in over half the animals (Figs. 3, 4).

In contrast to the right ventricular stroke volume, the left ventricular stroke volume did not increase with inspiration in any animal. However, the total aortic flow during inspiration increased in five of nine dogs, and decreased in none, since the heart rate increased in these five dogs (Table 1). The variance of stroke volume of the left ventricle was similar to that of the right: standard deviations from 5 to 16%, with lesser variance with tachycardia. In the individual animal, the variance in stroke volume for the two ventricles was quite similar. Even the individual stroke volumes of the left ventricle were closely covariant with the right; when the latter increased, the left ventricular stroke volume also increased either simultaneously, or at the latest, one or two beats after the increase on the right (Table 2).

Discussion

Venous flow. Pulsatile flow patterns in the vena cava and the pulmonary vein are quite similar, offering some support to the position that the vis a fronte (i.e., attraction into the heart) is more important in determining venous flow patterns than the transmitted, forward-flow pulse (vis a tergo). Considering that these veins empty immediately into a pump with intermittent ejection and filling, the action of the ventricle ahead of the respective vein should, a priori, produce a marked effect on the flow patterns in these veins.

Morkin et al. (8), offering a mathematical model as evidence, assert that the major flow pulse in the pulmonary vein is transmitted from the pulmonary artery but the pressure pulse is damped out completely by viscous

FIG. 4. Two records from the same dog obtained a few minutes apart demonstrating the variability of the flow pattern in the pulmonary vein with inspiration. On the left, the flow declines with inspiration, and on the right, increases. The latter pattern was found more consistently.
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FIG. 5. Detailed record demonstrating relationships of flows with respiration. Unfortunately the amplification of the intra-

TABLE 2. Correlation coefficients for aortic stroke volume (AoSV) against preceding diastolic interval

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Items</th>
<th>Preceding Interval</th>
<th>Corr. Coeff. (r)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>23</td>
<td></td>
<td>r = -.067</td>
<td>Good correl. between</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>AoSV_i/PaSV_i-2</td>
</tr>
<tr>
<td>16</td>
<td>15</td>
<td>r = .682</td>
<td></td>
<td>Tachycardia. Good correl.</td>
</tr>
<tr>
<td>31</td>
<td>26</td>
<td>r = .930</td>
<td></td>
<td>AoSV_i/PaSV_i</td>
</tr>
<tr>
<td>32</td>
<td>24</td>
<td>r = .161</td>
<td></td>
<td>Tachycardia. Good correl.</td>
</tr>
<tr>
<td>34a</td>
<td>25</td>
<td>r = .916</td>
<td></td>
<td>AoSV_i/PaSV_i-1 or i-2</td>
</tr>
<tr>
<td>34b</td>
<td>48</td>
<td>r = .882</td>
<td></td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>25</td>
<td>r = .547</td>
<td></td>
<td></td>
</tr>
<tr>
<td>39</td>
<td>32</td>
<td>r = .838</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In some animals with low or negative correlation coefficients, there were good correlations between the aortic stroke volume (AoSV_i) and the pulmonic stroke volume of one or two beats previously (PaSV_i-1 or PaSV_i-2).

Resistance through the capillary bed. Although no satisfactory physical models have been developed for the complex pulmonary circulation (1), it is unlikely that there would be such a drastic dissociation of the pressure and flow pulses in the pulmonary circuit (Caro (3) states that in small tubes, such as capillaries, pressure and flow are virtually in phase (10)). The only major positive-pressure pulse consistently found in the pulmonary vein (Fig. 3) is coincident with a retrograde-flow pulse, associated with atrial systole. The constant relationship in both venous systems of the forward-flow pulses to the ventricular events in the absence of pressure pulses makes the hypothesis of Morkin et al. quite unlikely considering the wide disparity in dimensions, impedances, and pressures in the systemic and pulmonary circuits.

We suggest that the systolic flow pulse in both the vena cava and pulmonary vein is due to descent of the atrioventricular valves with ventricular systole, which sucks blood into the atrium, and the diastolic flow pulse is due to the filling phase of the ventricles (2).

Respiratory effects. The events initiated by inspiration may be generalized in the following sequence. The negative intrathoracic pressure of inspiration causes an increased effective filling pressure of the right heart, demonstrated by a forward surge in the venae cavae, superimposed on the cardiac pulsations (Fig. 2). This surge is reflected within a beat or two by an increase in stroke volume from the right ventricle (Fig. 5). In most healthy animals, the heart rate also increases within the first one or two beats of inspiration, shortening the filling time for the ventricles. The shortened filling interval would probably reduce the stroke volume if it were not for the nearly simultaneous increase in venous flow to the right heart. Although the total pulmonary flow during inspiration (stroke volume X heart rate, calculated for each beat, and summed) was increased in almost every instance (Table 1), the right ventricular stroke volume rose in only one-half of the animals during inspiration. This effect of the increased heart rate on the stroke volume has been somewhat neglected in previous discussions of the changes in flow patterns with respiration. Part of the neglect may stem from acute experiments on animals which usually have some degree of tachycardia, or in unsedated animals sufficiently excited to produce tachycardia.

A somewhat surprising finding was an increase in flow
in the pulmonary veins during inspiration in over one-half the records (Fig. 4) in contrast to earlier predictions that blood would pool in the pulmonary veins (6). This increase in flow probably accounts for the associated increase in total aortic flow (stroke volume \times heart rate) in over one-half the animals during inspiration (Table 1), since an increase in heart rate without an increase in venous return would result in only a decrease in stroke volume. This inspiratory increase in pulmonary venous flow suggests a relatively short transit time of the inspiratory surge from the right heart, or alternatively that increasing the heart rate alone may produce acceleration of venous flow through ventricular suction (2).

As far as the variations in left ventricular stroke volume—as opposed to total aortic flow—are concerned, the filling interval seemed to have a more important effect than the inspiratory surge (Table 2). In 7 of 11 experiments, the correlation coefficients between the left ventricular stroke volume and the filling interval for the respective beat were quite high. Of the four instances with poor correlation for these variables, two were associated with tachycardia, which effectively eliminates variance in the filling interval and stroke volume. Three animals with poor correlation between the left ventricular stroke volume and filling interval demonstrated significant correlations between the left ventricular stroke volume and the right ventricular stroke volume of either the preceding beat \((i - 1)\) or of two beats prior \((i - 2)\), suggesting that the transit time of flow pulses from right to left ventricle through the pulmonary vascular bed was that of one or two beats. In the majority of animals, however, the effect of varying filling interval was more

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**FIG. 6.** Graph of the heart rate, stroke volume, and the stroke volume \(\times\) heart rate calculated for each beat of the right and left ventricles. Note that the variations in the stroke volumes of the two ventricles are in phase in this animal. (Shaded area represents inspiration.)

**FIG. 7.** Graph of same variables as in Fig. 6, but for a different animal. The variations in aortic stroke volume lag two beats behind those of the pulmonary artery. (Shaded area represents inspiration.)
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important in determining the stroke volume than was
the inspiratory surge.

It follows that in those instances in which filling interval is closely correlated with the left ventricular stroke volume, the stroke volume of the right ventricle would also correlate with that of the left ventricle. In Fig. 6, the heart rate calculated for each beat, the stroke volumes of the right and left ventricle, and the products of the respective stroke volume \( \times \) rate are graphed. The remarkable similarity of variation in stroke volume of the two ventricles is reflected also in a correlation coefficient of 0.79. The correlation coefficient for the left ventricular stroke volume and the preceding diastolic interval is very high, 0.90. This general relationship held for 7 of 11 experiments analyzed.

In Fig. 7, however, it is obvious by inspection that the cycle of aortic stroke volume lagged the pulmonic by two beats. This is substantiated by the correlation coefficient of 0.6495 between the aortic stroke volume and the pulmonic stroke volume of two beats prior \((i - 2)\), whereas the coefficients were \(-0.2721\) and \(-0.1367\) for the pulmonic beats just prior \((i - 1)\) and coincident \((i)\) with the aortic stroke volume, respectively. In this animal, the inspiratory surge and the delay of its transmission appeared to be more important determinants of aortic stroke volume than was the filling interval (coefficient of 0.1354 between the stroke volume and filling interval).

There are obviously other important determinants of stroke volume, some of them directly related to filling interval, such as the distending pressure of the ventricle. Other factors, less easily quantified, may be more primary than filling interval, such as cyclic variations in arteriolar resistance, venous capacitance, and even myocardial inotropism. We did not systematically measure distending pressure of the left ventricle, but as we have previously indicated, this requires the measurement of pericardial pressure; assuming identity of the pericardial pressure with intrathoracic pressure involves an error of 30–50\% with longer filling intervals (7).

From our data, the respiratory cycle affects the left ventricular stroke volume in at least two ways. In subjects with sinus arrhythmia, the acceleration of heart rate with inspiration shortens the ventricular filling time and tends to reduce the stroke volume. Second, inspiration produces a surge of venous flow into the right heart, which appears as an increased pulmonary venous flow within the interval of one or two heartbeats, in some instances overriding the effect of the changing heart rate.

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REFERENCES