Effects of Blood Flow and Left Atrial Pressure on Pulmonary Venous Resistance

By Kizuku Kuramoto, M.D., D. Med. Sc., and Simon Rodbard, M.D., Ph.D.

The contribution of the pulmonary venous system to the pulmonary vascular resistance has been a subject of increasing interest.\(^1\)\(^-\)\(^7\) The pulmonary veins are sometimes considered to consist of wide inactive vessels; however, histological studies have revealed a layer of smooth muscle in these veins, especially at their junction with the left atrium.\(^8\) The veins may also respond histologically by venous intimal fibrosis in chronically increased blood flow, as in atrial septal defect.\(^9\)

Some workers have, without measuring flow rates, interpreted an increase in the pressure gradient from the pulmonary vein or the pulmonary arterial wedge position to the left atrium as evidence for venous constriction.\(^2\)\(^,\)\(^6\) However, a change in gradient from pulmonary capillary or vein to left atrium does not necessarily indicate active venous constriction, since mechanical factors, such as blood flow or left atrial pressure, may also account for this increasing gradient. To be certain of such an interpretation, it would be necessary to measure the capillary pressure directly, but no means are available for such a direct measurement.

The arterial wedge pressure, which approximates the pressure in the left atrium or the large pulmonary veins,\(^10\)\(^-\)\(^17\) has been utilized as an estimate of the pulmonary capillary pressure.\(^13\)\(^,\)\(^14\) Theoretical objections\(^15\) and technical difficulties\(^12\)\(^,\)\(^16\)\(^-\)\(^18\) have raised serious questions concerning the use of arterial wedge pressure measurements as estimates of the pulmonary capillary pressure. Direct measurement of venular pressures with a small catheter may permit a more reliable estimation. As a step in this direction, we have examined the contribution of mechanical factors of blood flow and of the left atrial pressure on the pulmonary venular pressure and venous resistance.

Methods

Experiments were performed in thoracotomized dogs and in isolated lungs.

THORACOTOMY

Eleven dogs, 12 to 19 Kg., were anesthetized with intravenous pentobarbital (30 mg./Kg.). Under positive pressure respiration with 95 per cent O\(_2\) and 5 per cent CO\(_2\) through the Burns resuscitator valve (Pneophore), left thoracotomy was performed at the fourth costal interspace. Positive intrapulmonary pressure at a maximum of 6 mm. Hg inflated the lung; during deflation, the intrapulmonary pressure fell to 1 mm. Hg. After heparinization (5 mm./Kg.), cannulas were inserted into the pulmonary arterial trunk and into both main branches of the pulmonary artery in order to measure blood flow separately through each lung. A rotameter (Fischer and Porter Company) was placed between the pulmonary arterial trunk and each main branch of the pulmonary artery, taking care to preserve the innervation of the right lung. Flow through the right lung was modified by clamping either the right or left main branch of the pulmonary artery. Pressures were recorded from the following: (1) right pulmonary artery peripheral to the flowmeter; (2) right pulmonary venule via a small catheter introduced as far as possible into the pulmonary vein, the tip usually being 6 or 7 cm. from the junction of the atrium with the vein; (3) the left atrium. The venular catheter was introduced through a thin-walled glass tube inserted into the pulmonary vein via the left atrium. A vinyl catheter of 0.9 mm. O.D. and 0.5 I.D., or a polyethylene catheter with an O.D. of 0.6 mm. and an I.D. of 0.3 was used. The pulsatile pressure curves recorded through the 0.6-mm. catheter were somewhat damped in contour, but the mean pressure was equal to that of the larger catheter. Patency of the catheter tip was ensured by the observation of a rapid fall to control pressures within three seconds after injecting a small volume of saline.

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TABLE 1
Mean Pressures in the Pulmonary Artery (P_A), Venules (P_v), and Left Atrium (P_LA); Blood Flow in the Right Pulmonary Artery (RPA); and the Total Cardiac Output in Thoracotomized Dogs

<table>
<thead>
<tr>
<th>Dog number</th>
<th>Weight of dog (Kg)</th>
<th>P_A (mm Hg)</th>
<th>P_v (mm Hg)</th>
<th>P_LA (mm Hg)</th>
<th>Flow RPA (L/min.)</th>
<th>Cardiac output (L/min.)</th>
<th>Venous resistance (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.6</td>
<td>16.0</td>
<td>7.5</td>
<td>4.2</td>
<td>0.58</td>
<td>0.92</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>16.2</td>
<td>18.0</td>
<td>10.9</td>
<td>4.1</td>
<td>0.71</td>
<td>1.39</td>
<td>49</td>
</tr>
<tr>
<td>3</td>
<td>17.0</td>
<td>15.1</td>
<td>5.6</td>
<td>2.5</td>
<td>0.70</td>
<td>1.15</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>14.0</td>
<td>16.5</td>
<td>8.0</td>
<td>5.1</td>
<td>0.52</td>
<td>0.87</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>12.4</td>
<td>16.7</td>
<td>10.3</td>
<td>4.8</td>
<td>0.55</td>
<td>0.99</td>
<td>46</td>
</tr>
<tr>
<td>6</td>
<td>12.4</td>
<td>18.5</td>
<td>6.0</td>
<td>2.2</td>
<td>0.58</td>
<td>0.91</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>16.8</td>
<td>24.6</td>
<td>12.3</td>
<td>5.5</td>
<td>0.86</td>
<td>1.80</td>
<td>35</td>
</tr>
<tr>
<td>8</td>
<td>13.6</td>
<td>18.6</td>
<td>10.7</td>
<td>4.7</td>
<td>0.66</td>
<td>1.03</td>
<td>43</td>
</tr>
<tr>
<td>9</td>
<td>18.0</td>
<td>17.1</td>
<td>9.3</td>
<td>4.0</td>
<td>0.60</td>
<td>1.53</td>
<td>40</td>
</tr>
<tr>
<td>10</td>
<td>19.2</td>
<td>22.0</td>
<td>10.5</td>
<td>5.0</td>
<td>0.80</td>
<td>1.14</td>
<td>32</td>
</tr>
<tr>
<td>11</td>
<td>18.6</td>
<td>19.0</td>
<td>9.5</td>
<td>4.5</td>
<td>0.70</td>
<td>1.11</td>
<td>34</td>
</tr>
<tr>
<td>Mean</td>
<td>18.4</td>
<td>18.1</td>
<td>9.1</td>
<td>4.2</td>
<td>0.66</td>
<td>1.17</td>
<td>34</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>2.8</td>
<td>2.1</td>
<td>1.0</td>
<td>0.11</td>
<td>0.29</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Resistance (R) was calculated as the pressure drop (ΔP) divided by the blood flow (Q):

\[ R = \frac{\Delta P}{Q} \]

Pulmonary arterial pressure (P_A), pulmonary venular pressure (P_v), and left atrial pressure (P_LA) were used for the calculation of segmental resistance:

- total pulmonary vascular resistance = \( \frac{P_A - P_LA}{Q} \);
- artery and capillary resistance = \( \frac{P_A - P_v}{Q} \);
- venous resistance = \( \frac{P_v - P_LA}{Q} \).

Results

The results in the thoracotomized dogs and in the isolated lung experiments were essentially similar; venular pressures obtained with the two catheters with outside diameters of 0.9 mm. and 0.6 mm. were not significantly different.

Basal Conditions in the Thoracotomized Dog

The data are given in table 1. The mean pulmonary arterial pressure ranged from 15.1 to 24.6 mm. Hg, with a mean of 18.4 mm. Hg; the mean pulmonary venular pressure ranged from 5.6 to 12.3 mm. Hg, with a mean of 9.1; the mean left atrial pressure ranged from 2.2 to 5.5, with a mean of 4.2 mm. Hg. The pressure gradient from pulmonary venule to left atrium accounted for 23 to 50 per cent of the total gradient from the pulmonary artery to the left atrium.
EFFECT OF FLOW ON VENULAR PRESSURE AND VENOUS RESISTANCE

Twenty-six experiments were carried out on thoracotomized dogs, and 10 experiments were performed on excised lobes. Flow through the right pulmonary artery in the thoracotomized dogs was modified by gradually constricting the connection of the flowmeter to either the right or left main branch of the pulmonary artery. Severe constriction of one pulmonary artery sometimes decreased the total pulmonary blood flow to about 80 per cent of control levels, but the left atrial pressure remained unchanged. Representative tracings given in figure 1 show that pulmonary arterial and venular pressures diminish as flow decreases, while pressures in the pulmonary vein and left atrium remain unchanged. The pressure/flow relationship through the venous system was similar in contour to that of the total pulmonary vasculature; there was an almost linear relationship between venular pressure and flow except in the low ranges (fig. 2).

Thus, as flow was augmented, the calculated resistances decreased in the venous system as well as in the artery and capillary systems (fig. 3). When inflation pressure and left atrial pressure were held constant, the ratio of arterial and capillary resistances to the venous resistance was quite constant.

EFFECT OF LEFT ATRIAL PRESSURE ON VASCULAR RESISTANCE

In eight experiments on isolated lungs, the level of the venous outlet was raised from 0 to 20 mm. Hg, while the intra- and extrapulmonary air pressures and flow through the lung were held constant.

Figure 4 shows the typical changes of pressure gradients between (1) pulmonary artery and left atrium, (2) artery and venule, and (3) venule and left atrium. Since flow was constant, these gradients were proportional respectively to the resistances in (1) the total
pulmonary circulation, (2) the artery and the capillary, and (3) the venous system. A sharp decrease in venous resistance was seen as the left atrial pressure was elevated from control levels, and the effect then became less notable. Arterial and capillary resistance also fell gradually to a lesser extent. The total resistance therefore decreased sharply at first as left atrial pressure was elevated and then gradually leveled off.

The relationship between venular pressure and blood flow was essentially similar over a left atrial pressure range from zero to 15 mm Hg. However, as left atrial pressure was raised, the venular pressure approached that of the left atrium and the ratio of the venous resistance to the total pulmonary vascular resistance decreased.

Discussion

Our results in thoracotomized dogs and in isolated lungs indicate that the pressure gradient from the pulmonary venules to the left atrium may account for one-fourth to one-half of the total pulmonary vascular gradient. Thus, the pulmonary venous system contributes approximately one-third of the total pulmonary vascular resistance, and there is an almost linear relationship between pulmonary venular pressure and blood flow except in the low flow ranges.

An elevation of the left atrial pressure reduces the pulmonary vascular resistance primarily through its effect in decreasing the venous resistance. The artery and capillary resistances also decrease but to a lesser extent.

The problem of the measurement of the capillary pressure has led to numerous experiments and discussions. Aviado found that the venular pressure obtained with a small catheter with an outside diameter of 0.4 mm was about midway between that in the arteries and that in the large veins. He obtained higher venular pressures by pushing a smaller catheter into the pulmonary veins to points nearer the capillaries.

The pulmonary arterial wedge pressure is sometimes considered to represent the intra-capillary as well as the capillary venous pressure, since the contours obtained resemble those of the venous pulse. However, Connolly et al. and Wilson et al. have held that the pulmonary arterial wedge pressure is approximately equal to the mean left atrial pressure. Ankeney found that at the end of ventricular systole, the pulmonary arterial wedge pressure was 1.5 to 3.7 mm Hg higher than left atrial pressure. There have been similar discussions on the significance of the pulmonary venous wedge pressure. Wilson et al. and Haddy et al. noted a close relationship between the pulmonary venous wedge pressure and the mean pulmonary arterial pressure. But Connolly and Wood found the pulmonary venous wedge pressure in patients with atrial septal defect to be intermediate between pulmonary arterial and left atrial pressure. Attempts have been made to account for these discrepancies on the basis of various anesthetic conditions and underlying diseases, as well as the fact that some of the studies were in open-chest preparations while others were in closed chests. Recently, Aviado found that the venous wedge pressure in dogs.

Circulation Research, Volume XI, August 1964
Arterial, capillary, and venous vascular resistances calculated from figure 2.

Equaled the pulmonary arterial pressure only when a large catheter (O.D. 3.0 mm.) was used; a small catheter (O.D. 0.4 mm.) gave values intermediate between the arterial and the venous pressures.

In our experiments, small catheters were inserted as far as possible into a pulmonary venule. The rapid fall of pressure after injection of a small volume of fluid into these venular catheters demonstrated their patency, indicating that pressures obtained in this system represented those at the catheter tip; such pressures are not venous "wedge" pressures since these small flexible catheters are technically difficult to place in a "wedge" position. A larger catheter, which is relatively easy to wedge in a small artery, obstructs flow through the affected vascular segment, producing a static column from the catheter to the relatively large veins. The obstructed capillaries and venules will then represent an extension of the catheter to the large pulmonary veins. Thus, the pulmonary arterial wedge pressure represents the pressure in the large veins, and venous wedge pressure represents the arterial pressure; the pressure obtained by wedging the catheter from either the arterial or venous side may not reflect the true capillary pressure. A limiting factor of the wedge pressure technique is that hemodynamic and respiratory oscillations tend to dislodge the tip and permit leakage around the catheter.10

Several workers have called attention to the effect of blood flow on the pulmonary venous pressure. Werko et al.14 reported that changes in pulmonary arterial pressure did not affect the pulmonary arterial wedge pressure ("pulmonary capillary venous pressure"); however, it is likely that these workers were measuring pressures in the large pulmonary veins. By contrast, Haddy et al.21 found in man that the pulmonary venous pressure, measured 2 cm. peripheral from the left atrium, increased with the cardiac index. Aviado1 found such responses to blood flow increments when venular pressures were measured with very small (0.4 mm.) catheters. Eliakim and Aviado7 have recently described pressure-flow relationships of the extrapulmonary portion of the pulmonary vein; with increasing flow rates, they found a rise in pulmonary venous pressure (measured at the lung border or just inside the lung tissue) and a fall in extrapulmonary venous resistance. Our results also show that the venular pressure rises when either blood flow or arterial pressure is increased.

Since pulmonary venular pressure is affected by flow as well as by the pulmonary arterial pressures, a rise of venular pressure per se does not necessarily indicate venomanomation and a rise in venous resistance. It is clear that simultaneous measurements of the venous outflow and the pressure gradient across a vascular segment are necessary if the resistance of the venous beds is to be calculated; only when such data are in hand does it become possible to evaluate the resistance of the artery and capillary bed.

It is well established that an elevation of the left atrial pressure decreases the pulmonary vascular resistance.22-25 An essentially similar effect has been demonstrated in flow through collapsible vessels in which a rise in outlet pressure reduces the total resistance in the system.25, 27 The present study indicates

Circulation Research, Volume XI, August 1968
that this decrease is due in significant part to distention of the pulmonary venous system. Engelberg and DuBois have indicated that "more than 60 per cent of the compliance of the whole pulmonary vascular bed . . . resides in the venous tree." This large compliance may represent either distensibility or collapsibility of the pulmonary venous system.

If the pulmonary veins, which have the lowest intravascular pressures of the lesser circulation, are collapsed by slightly higher extravascular pressures, a slight elevation of the left atrial pressure may distend these vessels and effect a fall in venous resistance. The rise in the venous pressure may also raise the intraepithelial pressure and prevent collapse of these vessels.

High alveolar air pressures may collapse the blood vessels in the lung and thereby modify the distribution of the resistance in the arteries, capillaries, and veins. In the present study, insufflation pressure was maintained at levels which obviated the collapse, and the effect of air pressure was probably not of major importance.

The present results emphasize that a rise in venular pressure may reflect an increase in flow rather than a rising resistance in the venous system. Furthermore, the effect of mechanical factors, such as blood flow and left atrial pressure, must be considered in the evaluation of changes in pulmonary venous resistance.

Summary
Pulmonary venular pressure was measured in 11 thoracotomized dogs and in 8 isolated lung lobes by introducing a small catheter (O.D. 0.6 or 0.9 mm.) as far as possible retrograde into the pulmonary veins. In thoracotomized dogs, insufflated with a maximal air pressure of 6 mm. Hg, the mean pulmonary arterial, venular, and left atrial pressures averaged 18.4, 9.1, and 4.2 mm. Hg, respectively. An almost linear relationship was found between venular pressure and pulmonary blood flow, except in the low flow ranges; venular pressures exceeded left atrial pressure by one-fourth to one-half of the gradient from pulmonary artery to left atrium. The calculated pulmonary venous resistance decreased with increased blood flow. The fall in pulmonary vascular resistance resulting from elevation of the left atrial pressure was shown to reside primarily in the venous system, especially when left atrial pressure was low; arterial and capillary resistance also fell, but to a lesser extent. Pulmonary venular pressure is higher than left atrial pressure by a factor which varies with blood flow. The effect of such mechanical forces on the venous resistance is discussed.

References


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