Wave Transmission in the Pulmonary Arterial System in Disease in Man

By Stuart R. Reuben, M.B.

ABSTRACT

Pulmonary capillary blood flow was measured by the nitrous oxide-body plethysmograph technique in 21 patients with valvular heart disease or pulmonary thromboembolism during routine diagnostic cardiac catheterization. The studies were performed with a high-frequency phonocardiogram recorded from the pulmonary area to indicate the pulmonary valve opening at the beginning of right ventricular ejection. The pulmonary artery to capillary flow conduction time was measured from the time of pulmonary valve opening to the foot of the pulmonary capillary flow pulse. The conduction time was greater than 160 msec when the pulmonary artery pressure was normal. The fall in the conduction time in disease indicated elevated pulmonary arterial pulse wave velocity and this correlated well with the level of pulmonary arterial pressure (correlation coefficient 0.92, P < 0.001). This suggests that there is a reduced pulmonary arterial distensibility in the chronic pulmonary hypertension of valvular heart disease and thromboembolic disorders.

ADDITIONAL KEY WORDS pulmonary capillary flow pulse nitrous oxide-body plethysmograph flow conduction time pulmonary arterial distensibility z transform

Analog computer studies in a model (1) and studies in animals (2, 3) have suggested that the pulmonary capillary flow profile might be dependent on the elastic and transmission properties of the pulmonary arterial system. Furthermore, several groups of workers (3-5) have shown that the distensibility of the pulmonary artery of the dog, defined as the percent volume change in the system per unit change in pressure, is related to the level of pulmonary arterial pressure. Recently, Milnor and his colleagues (6) have shown that the phase velocity in the pulmonary artery of patients with valvular heart disease was elevated in those patients with pulmonary hypertension. This, they suggest, emphasizes the importance of reduced pulmonary arterial distensibility in the pulmonary hypertension of valvular heart disease.

The present paper describes an attempt to correlate flow wave transmission in the pulmonary arterial system with pulmonary arterial pressure in patients with pulmonary arterial hypertension. The pulmonary capillary flow pulse was used to detect the arrival of the right ventricular ejection pulse at the gas-exchanging vessels. It was hoped that the demonstration of such a correlation might confirm reduced pulmonary arterial distensibility in pulmonary hypertension by an indirect method and also demonstrate the usefulness of the N2O-body plethysmograph technique for the repeated, nontraumatic study of patients.

Subjects and Methods

The studies were performed with data obtained from 21 patients with valvular heart disease or pulmonary thromboembolism, who had undergone diagnostic cardiac catheterization and simultaneous N2O-body plethysmography. The hemodynamic data from 16 of these patients has already been presented for other purposes (7). All the patients were in sinus rhythm. Details of the patients, including diagnosis and anthropometric data, are shown in Table 1.

The patients lay on the body plethysmograph couch, which was fully withdrawn from the chamber and placed beneath an image-intensifier.
A double-lumen catheter was introduced into the pulmonary artery from a right antecubital vein. Pulmonary arterial and pulmonary arterial "wedge" pressures, the latter taken as an indirect measurement with Statham P23Gb strain-gauge "wedge" pressures, were measured by the Fick principle using a 5-minute expired gas collection (9). The pattern of instantaneous N₂O uptake and thus of pulmonary capillary blood flow was obtained by algebraically subtracting the plethysmograph gas flow record during the exhalation following an inhalation of air, from the record obtained after a similar inhalation of 80% N₂O in oxygen (Fig. 1). All patients were trained to perform the respiratory maneuver repeatedly in an identical manner and to maintain constant air flow during slow exhalation. The pulmonary artery to capillary flow conduction time (ct in Fig. 1) was measured as the interval between the third major vibration of the first heart sound (S₃) and the foot of the capillary flow pulse. In patients in sinus rhythm no difficulty was encountered in delineating the foot of the pulmonary capillary flow pulse, and measurements made by different observers usually agreed within 10 msec.

**Results**

Figure 2 shows a graph of pulmonary artery to capillary conduction time (ordinate) against the mean pulmonary arterial pressure for each patient (abscissa). The relationship shown is an inverse curvilinear one and suggests that the patients with the severest disease and most marked pulmonary hypertension had the shortest flow conduction times.

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1Statham Scientific Instrument Co., California, U.S.A.

2Beckman Physiological Gas Analyzer, Model LB-1, Palo Alto, California, U.S.A.

A curvilinear regression equation was obtained for this data using a z transform (Appendix). The relationship between pulmonary artery-capillary flow conduction time ($ct$) and mean pulmonary arterial pressure ($P$) was given by the equation

$$ct = 31 + \frac{1910}{P^2}.$$  \hspace{1cm} (1)

**Discussion**

Karatzas and Lee (7) have recently shown the importance of pulmonary arterial and venous resistance and heart rate on the pulmonary capillary flow profile in patients with valvular heart disease. Furthermore, the studies of Engelberg and DuBois (2), Wasserman et al. (1) and Reuben et al. (3) have suggested that the distensibility properties of the pulmonary arteries are also of importance in determining the pattern of pulmonary capillary blood flow. Bramwell and Hill (17) have shown that the pulse wave velocity in a vessel is related to the distensibility of the vessel walls.

Thus:

$$c_0 = \frac{\Delta P \times V_o \times g}{\sqrt{\Delta V \times \rho}},$$  \hspace{1cm} (2)

where $c_0$ = P.A. pulse wave velocity (cm/sec), $V_o$ = total volume of the P.A. system (ml), $\Delta P$ = change in distending pressure in the system (mm Hg), $\Delta V$ = corresponding change in volume of the system (ml), $g$ = gravitational acceleration (g-cm/sec²), and $\rho$ = density of blood (g/ml).

The capillary flow pulse recorded by the N₂O method represents the instantaneous summation of the flow pulses in all capillaries.
engaged in gas exchange. In a manner similar to Karatzas and Lee (18), the pulmonary capillary flow pulse recorded in these studies has been taken to correspond to the pattern of outflow of blood from the pulmonary arterial system. It is assumed that there is a matching of the length of the various vascular pathways to their conduction properties so that pulse wave velocity is effectively uniform through all of them. Therefore, the time delay from the beginning of right ventricular ejection (pulmonary valve opening) to the foot of the capillary flow pulse has been taken to represent the conduction time of the flow pulse.

The pulse wave velocity can be calculated from the time interval from pulmonary valve opening to the foot of the pulmonary capillary flow pulse and the mean path length.

Thus: \[ c_o = \frac{\text{mean PA - PC path length}}{\text{PA - PC flow conduction time}} \] (3)

In these clinical studies it was not possible to estimate the mean pulmonary artery (PA)-pulmonary capillary (PC) path length. However, calculations based on equations 2 and 3 using the animal data of Reuben et al. (3) show that the mean path length, in dogs with acute pulmonary hypertension, induced either by hypoxic ventilation or serotonin infusion increased insignificantly from the control value. Similarly, calculations based on the impedance and phase velocity data of Milnor (6) show that, if anything, the pulmonary artery-capillary path length increases in the
pulmonary hypertension of valvular heart disease.

However, the close correlation between mean pulmonary arterial pressure and conduction time (Fig. 2 and Table 2) seems to indicate that, despite the fact that no account was taken of patient size and vascular geometry, the flow conduction time depends on the distensibility of the pulmonary arterial system and hence on the level of pulmonary arterial pressure. On the basis of equation 3, the data shown in Figure 2 suggest that the pulmonary arterial pulse wave velocity \(c_o\) is greatly elevated in the pulmonary hypertension of valvular heart disease and pulmonary thromboembolism. This elevated pulse wave velocity must be due to a reduced pulmonary arterial distensibility (equation 2). These findings are in close agreement with those of Caro and Harrison (19). It seems, therefore, that in the pulmonary hypertension of valvular heart disease and pulmonary thromboembolism, the human pulmonary arterial system behaves in a similar manner to that of dogs in acute studies (3), namely that it

### Table 2

<table>
<thead>
<tr>
<th>Patient</th>
<th>Heart rate (beats/min)</th>
<th>Cardiac output (liter/min)</th>
<th>Mean P.A. pressure (mm Hg)</th>
<th>(ct) (msec)</th>
<th>(P-P')</th>
<th>(ct-ct')</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.P.</td>
<td>81</td>
<td>6.6</td>
<td>15*</td>
<td>180*</td>
<td>0</td>
<td>-22.0</td>
</tr>
<tr>
<td>B.B.</td>
<td>44</td>
<td>4.4</td>
<td>15</td>
<td>160</td>
<td>0</td>
<td>-20.0</td>
</tr>
<tr>
<td>S.C.</td>
<td>71</td>
<td>3.6</td>
<td>18</td>
<td>60</td>
<td>3.0</td>
<td>-120.0</td>
</tr>
<tr>
<td>G.F.</td>
<td>60</td>
<td>3.8</td>
<td>18</td>
<td>90</td>
<td>15.0</td>
<td>-90.0</td>
</tr>
<tr>
<td>E.H.</td>
<td>85</td>
<td>3.8</td>
<td>18</td>
<td>140</td>
<td>8.0</td>
<td>-60.0</td>
</tr>
<tr>
<td>C.W.</td>
<td>90</td>
<td>3.5</td>
<td>30</td>
<td>100</td>
<td>15.0</td>
<td>-80.0</td>
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<tr>
<td>R.R.</td>
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<td>10.0</td>
<td>25</td>
<td>120</td>
<td>10.0</td>
<td>-60.0</td>
</tr>
<tr>
<td>S.H.</td>
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<td>3.2</td>
<td>23</td>
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</tr>
<tr>
<td>J.W.</td>
<td>90</td>
<td>3.0</td>
<td>30</td>
<td>100</td>
<td>15.0</td>
<td>-80.0</td>
</tr>
<tr>
<td>W.M.</td>
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<td>3.7</td>
<td>40</td>
<td>70</td>
<td>25.0</td>
<td>-110.0</td>
</tr>
<tr>
<td>P.W.</td>
<td>90</td>
<td>3.0</td>
<td>23</td>
<td>120</td>
<td>8.0</td>
<td>-60.0</td>
</tr>
<tr>
<td>P.C.</td>
<td>75</td>
<td>6.1</td>
<td>41</td>
<td>80</td>
<td>20.0</td>
<td>-100.0</td>
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<tr>
<td>H.C.</td>
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<td>6.5</td>
<td>34</td>
<td>100</td>
<td>19.0</td>
<td>-80.0</td>
</tr>
<tr>
<td>V.I.-Z.</td>
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<td>45</td>
<td>80</td>
<td>30.0</td>
<td>-100.0</td>
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<td>33</td>
<td>100</td>
<td>18.0</td>
<td>-80.0</td>
</tr>
<tr>
<td>E.C.</td>
<td>72</td>
<td>4.5</td>
<td>30</td>
<td>100</td>
<td>15.0</td>
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<td>S.L.</td>
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<td>50</td>
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</tr>
<tr>
<td>M.W.</td>
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<td>4.1</td>
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<td>90</td>
<td>21.0</td>
<td>-90.0</td>
</tr>
<tr>
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<td>47</td>
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<td>-103.0</td>
</tr>
<tr>
<td>G.M.</td>
<td>76</td>
<td>5.0</td>
<td>17</td>
<td>160</td>
<td>2.0</td>
<td>-20.0</td>
</tr>
<tr>
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<td>4.1</td>
<td>16</td>
<td>160</td>
<td>1.0</td>
<td>-20.0</td>
</tr>
</tbody>
</table>

*Represents the pair of variables which were selected as \(P'\) and \(ct'\); \(ct\) = pulmonary artery to capillary flow conduction time.

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becomes stiffer as the transmural pressure within the system becomes elevated.

Finally, the close correlation of pulmonary artery to capillary flow conduction time with mean pulmonary arterial pressure suggests that the N₂O-plethysmograph method may be useful as a noninvasive technique of estimating pulmonary arterial pressure with a surprising degree of accuracy.

Appendix

USE OF THE Z-TRANSFORM

One pair of variables is selected and denoted as P' and ct' (Table 2). No mathematical significance is attached to the selection. Columns 5 and 6 of Table 2 show the calculated values of (P-P') and (ct-ct'), respectively. Column 7 shows the value of Z, which is the ratio of (P-P') to (ct-ct'), for each pair of variables. A graph is then drawn (Fig. 3) of Z, on the ordinate, against the original value of P on the abscissa and linear regression analysis is performed to determine the intercept and slope of the linearized data.

The general equation for an inverse curvilinear function is:

\[ ct = a + \frac{b}{P + d}, \]  

where \( ct = PA - PC \) flow conduction time (msec), \( P = \) mean pulmonary arterial pressure (mm Hg), and a, b, and d are constants.

Now \( a = ct' + \frac{1}{S} \),

\[ S = \text{slope of the linear regression (Fig. 3)}, \]

\[ b = -\left(\frac{1}{S}\right)\left(P' + \frac{1}{S}\right), \]

where \( I = \text{intercept on the ordinate of the linear regression, and } d = \frac{1}{S}. \)

For the data shown in Table 2, \( I = 0.149 \), and \( S = -0.00673. \)

The correlation coefficient, r, of the linear regression (Fig. 3) was 0.92 (se = 0.00085) and this was highly significant (t = 10.33).

References


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