Capillary pressure and distribution of vascular resistance in isolated lung

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Agostoni, Emilio, and Johannes Piiper. Capillary pressure and distribution of vascular resistance in isolated lung. Am. J. Physiol. 202(6): 1033-1036. 1962. Isolated lobes of dogs' lungs were perfused with constant nonpulsatile blood flow and expanded by negative external pressure. The pressure under which Ringer solution was absorbed through the visceral pleura was measured by an osmometric method. From this pressure and the plasma colloid osmotic pressure, the pressure in the subpleural capillaries was calculated. The average value of the latter was 8.8 mm Hg when the pulmonary artery and vein pressures were 13.4 and 1.8 mm Hg, respectively. Assuming that the pressure in the intrapulmonary capillaries is similar to that in the subpleural capillaries, the vascular resistance on the arterial and venous side of the effective midpoint of pulmonary capillaries could be calculated. The average vascular resistance on the venous side was found to be 60% of the total intrapulmonary vascular resistance. Notwithstanding the limitations of the method this result suggests that in the pulmonary vascular bed the resistance on the arterial side and that on the venous side of the effective midpoint of capillaries are similar.

In a previous publication (1) a method was devised to study the absorption of Ringer solution through the visceral pleura in open-chest dogs. The approach for measuring the pressure under which the Ringer solution was absorbed consisted essentially in the application of an osmometer to the surface of the lung lobe. The semipermeable membrane of this osmometer was made up by the pleura and the wall of the capillaries lying under it. The pressure under which the Ringer solution was absorbed was given by the difference between the plasma colloid osmotic pressure and the mean pressure in the subpleural pulmonary capillaries.

In open-chest dogs ventilated by a pump at positive pressure the pulmonary capillary pressure, relative to atmospheric pressure, is higher than in physiological conditions when the alveolar pressure is oscillating around zero. By applying the above-mentioned method to isolated, perfused lungs, expanded by external negative pressure, the capillary pressure can be measured at zero alveolar pressure. Furthermore, in this preparation the pressures in the pulmonary artery and in the pulmonary vein, as well as the blood flow, can easily be controlled.

At given arterial and venous pressures the mean capillary pressure is determined by the distribution of vascular resistance to the arterial and venous sides of the point corresponding to the mean capillary pressure. (For this point we use the term, introduced by Pappenheimer and Soto-Rivera (2), "effective midpoint of capillaries"). Therefore, assuming that the pressure in the subpleural capillaries is similar to that in the intrapulmonary capillaries, the distribution of pulmonary vascular resistance can be calculated from experimental data.

Thus the purpose of this study is 1) to determine the net pressure under which the Ringer solution is absorbed through the visceral pleura of isolated, perfused lungs with physiological values of alveolar and vascular pressures, in order to compare these data to those previously obtained in situ on open-chest dogs, and 2) to determine the capillary pressure in isolated lungs perfused by constant flow and with physiological values of pulmonary arterial and venous pressures, for estimating the distribution of resistance to flow in the pulmonary vascular bed.

METHODS

All experimental dogs were anesthetized with 2 mg/kg morphine subcutaneously, 80 mg/kg chloralose, and 250 mg/kg urethan intravenously. Immediately after bleeding the lung-donor dog to death the left or right inferior lobe of the lung was isolated and connected to the perfusion system (Fig. 1). The lobe was perfused with arterial blood from the femoral artery of another large dog (21–26 kg) by a pump providing a nonpulsatile adjustable flow. The outflow from the lobe was led via a graduated container, where it could be measured, into the femoral vein of the dog. The blood flow and the outflow level were adjusted in such a way

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that the arterial pressure (Pa) was about 15 mm Hg and the venous pressure (Pv) about 2 mm Hg. The blood pressures were measured with water manometers at the entrance of the artery and of the vein into the lobe, the difference between the two pressures being therefore due only to the intrapulmonary vascular resistance. The lung lobe was suspended from the cover of a container in which a constant negative pressure (Pi) of about 6 mm Hg was maintained to keep the lung expanded. The temperature of the inflowing blood and of the moist air in the container was kept at 37 C by thermostats.

The osmometer for measuring the pressure under which the Ringer solution was absorbed through the visceral pleura was the same as that previously described in detail (I). The composition of the solution used was: 9 g NaCl, 0.3 g KCl, 0.25 g CaCl2, and 0.2 g NaHCO3 per 1 liter H2O. The apparatus was fastened to the cover of the container by an adjustable support. The graduated glass capillary for measuring the movement of the Ringer solution was not directly attached to the osmometer chamber but connected to it through a relatively undistensible tube that permitted us to keep the capillary outside the container and to change its level (Fig. 1).

The apparatus was applied to the isolated lung lobe which was expanded by a positive alveolar pressure of about 6 mm Hg during application of the apparatus. The blood flow was momentarily stopped and the cover with the attached lobe was placed in such a way that the osmometer cup could be applied to the lobe in horizontal position from below, as previously described for lungs in situ (I). After application of the apparatus the lobe was closed into the container and the perfusion resumed. Then the transition to negative pressure inflation was performed. The pressure inside the container was made progressively more negative (down to 6 mm Hg), while the intrapulmonary pressure was simultaneously lowered to atmospheric.

The glass capillary was always kept below the center of the osmometer cup, which was taken as zero level for all pressures (Fig. 1). After the temperature in the container had reached an equilibrium the movement of the liquid in the glass capillary was recorded for some minutes, until a steady movement was observed. Such measurements were repeated with the glass capillary at different levels. The flow of liquid through the membrane was then plotted against the negative pressure applied to the apparatus as given by the level of the glass capillary (taking into account the pressure due to the capillarity). From the plot the pressure at which no transfer of liquid occurred (Po) was determined. Po was considered as the net pressure under which the Ringer solution was absorbed into the subpleural capillaries.

In order to measure the plasma colloid osmotic pressure (π) the blood flow was stopped and the arterial and venous pressures were set at 8-10 mm Hg. Since there was no flow this was assumed to be also the value of the pressure in the pulmonary capillaries (Pc). The absorption pressure (Po) in this condition was determined as described above. The plasma colloid osmotic pressure was calculated as π = Pc + Po.

When Po during perfusion and π had been measured, Pc during perfusion could be obtained as Pc = π - Po.

From the values of pulmonary arterial, capillary, and venous pressures (Pa, Pc, and Pv) the distribution of the vascular resistance to the arterial and venous side of the effective midpoint of capillaries could be determined, assuming that the pressure measured in the subpleural capillaries was similar to that in the intrapulmonary capillaries. Since the total pulmonary vascular resistance is (Pa - Pv)/Q, the resistance on the arterial and venous side of the effective midpoint of capillaries is respectively given by (Pa - Pc)/Q and (Pc - Pv)/Q. The ratios (Pa - Pc)/(Pa - Pv) and (Pc - Pv)/(Pa - Pv) represent the distribution of pulmonary vascular resistance relative to the effective midpoint of capillaries.

As it takes about 1 hr to measure Po and π, this technique does not seem suitable for systematic study of changes in distribution of the pulmonary vascular resistance produced by changes in respiratory gas tensions or by vasoactive substances (see Discussion). Only in two lobes (exp. 1 and 3) was edema found at the end of the experiments which, in these cases, lasted more than 2 hr.

RESULTS

The data obtained in seven isolated lung lobes are reported in Table 1. With the mean arterial pressure of

![Diagram of the experimental setup for measurement of the pressure under which Ringer solution is absorbed through the visceral pleura of isolated, perfused lung lobes.](image-url)
solution through the visceral pleura was found to be 0.6, i.e., 60% of the total intrapulmonary pressure. From the osmotic pressure of 20.6 mm Hg, gives a mean pressure of the membrane could have been increased by the extracellular colloid membrane. Furthermore, the permeability of the membrane to be slightly lower than that found with a collodion membrane. The mean value of the plasma colloid osmotic pressure in the interstitial fluid has been found to be particularly low value in experiment I by this factor.)

The pressure in the subpleural capillaries could be different from that in the other pulmonary capillaries, because, according to morphological studies (7), the structure of the subpleural vessels differs from that of the intrapulmonary vessels. However, the magnitude and even the direction of this possible difference between the pressure in the intrapulmonary and subpleural capillaries cannot be appreciated.

The mean inward flow of Ringer solution was 1.2 × 10⁻² ml/min/mm Hg and per cm² of pleural surface, i.e., about two times as high as found in situ with positive alveolar pressure (1). The scatter is large (0.3–3.4), as previously found, and possibly related to the different characteristics of the membrane in the individual experiments. In one lobe showing macroscopic signs of disease no transfer of Ringer solution could be achieved; it is likely that some pathological processes had rendered the visceral pleura impermeable to water.

Our values can hardly be compared to the permeability values found by Landis (4, 5) for the frog mesentery, or by Pappenheimer and Soto-Rivera (2) and Pappenheimer (6) for perfused hind legs of cats and dogs, because their values are referred to the capillary surface area and probably only the capillary wall is concerned, whereas in our experiments Ringer solution had to pass capillary wall and pleural tissue, and our values are referred to the pleural surface covered by the osmometer cup, which is probably much larger than the effective capillary surface area.

The mean capillary pressure, Pc = 8.8 mm Hg, agrees with that previously found in situ after correcting for the positive alveolar pressure (1). The pressure in the subpleural capillaries could be different from that in the other pulmonary capillaries, because, according to morphological studies (7), the structure of the subpleural vessels differs from that of the intrapulmonary vessels. However, the magnitude and even the direction of this possible difference between the pressure in the intrapulmonary and subpleural capillaries cannot be appreciated.

If the pressure in the intrapulmonary capillaries is assumed to be equal to that of the subpleural capillaries, the vascular resistance on the arterial and venous side of the effective midpoint of capillaries can be calculated from the values for pulmonary arterial, capillary, and venous pressures. Under this assumption the results indicate that the resistance on the arterial side is 40% and on the venous side, 60% of the total intrapulmonary vascular resistance. It has been previously shown (8) by comparing the site of the resistance to flow to that of the pulmonary capillaries, that the pulmonary vas-

### Table 1. Experimental data for determination of capillary pressure and distribution of vascular resistance in isolated perfused lung lobes of dogs*

<table>
<thead>
<tr>
<th>Exp. No.</th>
<th>Lung Donor</th>
<th>Blood Flow (Q), ml/min</th>
<th>Intrathoracic Pressure (Pt), mm Hg</th>
<th>Plasma Colloid Osmotic Pressure (Pc), mm Hg</th>
<th>Absorption Pressure (PD), mm Hg</th>
<th>Capillary Pressure (Pc), mm Hg</th>
<th>Arterial Pressure (Pa), mm Hg</th>
<th>Venous Pressure (Pv), mm Hg</th>
<th>Pc/Pa - Pv</th>
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<td>9.6</td>
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* Left inferior lobe in exp. 2–6; right inferior lobe in exp. 1 and 7.†Mean values of arterial (Pa), capillary (Pc), and venous pressure (Pv) are referred to the pleural surface covered by the osmometer cup, which is probably much larger than the effective capillary surface area.

**Note:** The table provides experimental data for determining capillary pressure and the distribution of vascular resistance in isolated perfused lung lobes of dogs. It includes columns for Exp. No., Lung Donor Weight (Wt.), Blood Flow (Q), Intrathoracic Pressure (Pt), Plasma Colloid Osmotic Pressure (Pc), Absorption Pressure (PD), Capillary Pressure (Pc), Arterial Pressure (Pa), Venous Pressure (Pv), and the ratio of Pc/Pa - Pv. The data are presented for different experimental conditions, with results showing variations in pressure and resistance values.
cicular resistance was roughly coincident with the capillaries, but that the resistance on the arterial side of the capillary midpoint was somewhat larger than that on the venous side. As in the present experiments $P_c$ could not be measured more accurately than $\pm 1\text{ mm Hg}$, the ratio $(P_c - P_v)/(P_a - P_v)$ could be estimated only with an accuracy of about 10%. The method previously used to study the distribution of pulmonary vascular resistance (8) was no more accurate. Hence, considering the results and the accuracy of both methods, based on completely different approaches, it seems that the intrapulmonary vascular resistance is similar on the arterial and venous side of the effective midpoint of capillaries. In both these series of experiments a nonpulsatile flow has been used; whether the distribution of the intrapulmonary vascular resistance is similar when there is a pulsatile flow, as in physiological conditions, cannot be predicted.

As can be seen from Table I, there is a wide scatter of the values of the intrapulmonary vascular resistance (even after taking into account the weight of the dog), which is probably related to the condition of the isolated lung. For the lungs of the same dog the intrapulmonary vascular resistance of the right inferior lobe (exp. 7) was twice that of the left inferior lobe (exp. 6—both inferior lobes have roughly the same size). The experiment on the right lobe was performed 3 hr after isolating it, while the experiment on the left lobe was performed immediately thereafter. It had been previously noticed (9) that the vascular resistance of the isolated lungs increases if the lung is not perfused within a short time after its excision. However, the data in Table I do not show a relationship between the magnitude of the intrapulmonary vascular resistance and its distribution to the arterial and venous side of the effective midpoint of capillaries.

A few determinations of the distribution of the pulmonary vascular resistance have been made on the basis of measurement of the "wedge pressure" (10), which is supposed to represent the pulmonary capillary pressure. From the data of Kuida et al. (11) the values of the ratio $(P_c - P_v)/(P_a - P_v)$ are 0% in one dog and 10.5% in another dog, after injection of endotoxin these values increased to 32% and 79%, respectively. From the data of Rivera-Estrada et al. (19) the mean value of this ratio in five dogs was 8.5%, increasing to 56% after 20 min of hypoxia. These results suggest that the vascular resistance on the venous side is normally small as compared to that on the arterial side, but that in particular conditions (and even in isolated lungs, 11) the resistance on the venous side may become similar to that on the arterial side. A critical evaluation of the data obtained in the present and previous study (8) as compared to those derived from wedge pressure measurements can hardly be attempted because the wedge pressure does not necessarily represent the capillary pressure (13).

The distribution of vascular resistance in the systemic circulation has been determined, with a method similar in principle to that used in this study, by Pappenheimer and Soto-Rivera (2). In the hind leg of the cat the vascular resistance on the arterial side of the effective midpoint of capillaries was found to be 90%, and that on the venous side 10% of the total resistance.

One would like to attribute a functional significance to this marked difference in the distribution of vascular resistance between the systemic and the pulmonary vascular bed, as revealed by the results of Pappenheimer and Soto-Rivera, and of the present study. Certainly in the systemic circulation the high resistance on the arterial side of the capillaries is needed for the purpose of regulation of the distribution of the cardiac output according to the local needs, without excessive changes in the capillary pressure. On the other hand, one may search for reasons for the relatively high venous resistance in the pulmonary vascular bed. If there exists a critical closing pressure (14) for the pulmonary capillaries (experimental evidence in 9) the transmural pressure necessary to avoid capillary collapse can be secured only by a relatively high venous resistance. This feature could therefore render the pulmonary capillary bed more stable, especially in the case of increasing alveolar pressure.

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REFERENCES