Anatomic distribution of pulmonary vascular compliance

ROBERT G. PRESSON, J R., SAID H. AUDI, CHRISTOPHER C. HANGER, GERALD M. ZENK, RICHARD A. SIDNER, JOHN H. LINEHAN, WILTZ W. WAGNER, J R., AND CHRISTOPHER A. DAWSON

Departments of Anesthesia, Physiology/ Biophysics, Pediatrics, and Surgery, Indiana University School of Medicine, Indianapolis, Indiana 46202; Department of Physiology, Medical College of Wisconsin, Milwaukee 53226; Research Service, Zablocki Veterans Affairs Medical Center, Milwaukee 53295; and Department of Biomedical Engineering, Marquette University, Milwaukee, Wisconsin 53233

Presson, Robert G., J r., Said H. Audi, Christopher C. Hanger, Gerald M. Zenk, Richard A. Sidner, John H. Linehan, Wiltz W. Wagner, J r., and Christopher A. Dawson. Anatomic distribution of pulmonary vascular compliance. J. Appl. Physiol. 84(1): 303–310, 1998.—Previously, the pressure changes after arterial and venous occlusion have been used to characterize the longitudinal distribution of pulmonary vascular resistance with respect to vascular compliance using compartmental models. However, the compartments have not been defined anatomically. Using video microscopy of the subpleural microcirculation, we have measured the flow changes in ~40-µm arterioles and venules after venous, arterial, and double occlusion maneuvers. The quasi-steady flows through these vessels after venous occlusion permitted an estimation of the compliance in three anatomic segments: arteries >40 µm, veins >40 µm, and vessels <40 µm in diameter. We found that ~65% of the total pulmonary vascular compliance was in vessels <40 µm, presumably mostly capillaries. The transient portions of the pressure and flow data after venous, arterial, and double occlusion were consistent with most of the arterial compliance being upstream from most of the arterial resistance and most of the venous compliance being downstream from most of the venous resistance.

pulmonary microcirculation; arterial occlusion; venous occlusion; double occlusion; video fluorescence microscopy; digital image analysis; fluorescently labeled red blood cells; vascular resistance; mathematical model; isolated dog lung

PULMONARY ARTERIAL and venous occlusions have been used to characterize the longitudinal distribution of pulmonary vascular resistance with respect to compliance between the arterial and venous sites of occlusion (1–3, 6, 9–12, 18). The data obtained have been the time-varying arterial and venous pressures after occlusion. Various models (generally compartmental) have been used to interpret these data in terms of the distribution of compliance and resistance (2, 9, 11, 12). The process of determining the model elements needed to explain the data has provided insights into the mechanics of the pulmonary vascular bed. However, the identification of the arterial or venous sites of changes in vascular resistance and compliance and a determination of the pulmonary capillary pressure have been primary objectives of many of the studies. Such structure-function correlations have been based primarily on the observation that vasoconstrictor stimuli affect the model parameters in ways consistent with their known arterial or venous sites of action (2, 6, 12, 16). These correlations then provide the basis for interpreting the effects of stimuli having unknown sites of action. There are also other kinds of indirect evidence linking model parameters and anatomy, e.g., comparison of the compartmental nodal pressures with pressures estimated by other methods (6, 11, 18). The interpretations of these results have varied (2).

We have added the measurement of flow in subpleural arterioles and venules after vascular occlusion as an additional source of information linking structure and function. The flows were measured in isolated dog lung lobes under zone 3 conditions by using video microscopy to track fluorescently labeled red blood cells in vessels with diameters of ~40 µm. Under the assumption that fractional changes in flow in these vessels are representative of the fractional changes in flow in similarly sized vessels throughout the lungs, these arteriolar and venular flows allow for a direct, i.e., model-independent, estimation of the compliances of the arteries, capillaries, and veins from the flow response to venous occlusion. The rationale is that when the venous outflow is occluded while arterial inflow remains constant, the axial flow observed at any site between the inlet and the site of occlusion will be the inflow rate minus the rate of volume storage in the distensible vessels upstream from the site of observation. Because the rate of change in pressure at all locations within the system will be equal once the quasi-steady state has been established and because compliance is the change in volume for a given change in pressure, the rate of upstream volume storage over total flow is equal to the ratio of upstream compliance to total compliance. If the total compliance is estimated by measuring the change in pressure resulting from the total volume stored in the system up to a given time, the actual compliance of the segments upstream and downstream from the sites of observation, in this case ~40-µm subpleural arterioles and venules, can be calculated.

Using the compressions calculated from the flow data after venous occlusion and the pressure measured after simultaneous occlusion of arterial inflow and venous outflow (double-occlusion pressure), we used a previously described three-capacitor-two-resistor (3C2R) compartmental model representation of the lobar vascular bed (2) (Fig. 1) to calculate the longitudinal distribution of vascular resistance and determine its relationship to the distribution of compliance.

http://www.jap.org
METHODS

Experimental preparation. Adult, male, mongrel dogs (n = 6, 19–25 kg) were sedated with acepromazine (10 mg im), and 100 ml of blood were withdrawn from each animal by venipuncture. By use of techniques described in detail elsewhere (19), the red blood cells were fluorescently labeled with DiI16(3) and then reinfused. A 1-day delay was allowed to permit removal of any cells damaged during the labeling process. On the day after labeling, the animals were anesthetized by intravenous injection of pentobarbital sodium (30 mg/kg) freshly dissolved in 0.9% saline that was supplemented by 5 mg/kg doses as needed to maintain surgical anesthesia, intubated, and ventilated with air via a constant-volume respirator (model 607D, Harvard Apparatus). At that time, flow cytometry showed that 2–3% of the circulating red blood cells were fluorescently labeled. After heparinization (1,000 U/kg) the animals were rapidly exsanguinated through a cannula (3 mm ID) placed in the left common carotid artery. During the exsanguination, 150 ml of 10% dextran (70 kDa) in saline were infused (6). With the lungs inflated to a constant airway pressure of 4 mmHg, the left chest wall and the left upper lobe were excised to provide access to the left lower lobe. The left lower lobar artery was cannulated with a Teflon FEP cannula (6 mm ID), and the left lower lobe bronchus was clamped to maintain constant inflation. The left lower lobe was then excised along with a cuff of left atrium and placed on a microscope stand. The surface of the lobe was kept moist with saline throughout the procedure. The left atrial cuff was secured around another Teflon FEP cannula (10 mm ID), and the lobe was perfused with autologous, heparinized whole blood (hematocrit 31 ± 3%). Care was taken to exclude all air bubbles from the circuit before initiation of perfusion. The time interval from complete exsanguination to reperfusion of the lobe was ~25 min. Blood was pumped (model 7522–10 pump drive and model 7024–20 pump head, Masterflex) through a pulse dampener to reduce pump vibrations and trap bubbles, a filter (20-µm pore size, model 4C2423, Fenwal) to remove microaggregates, and a heat exchanger (model HE-100, Bentley) to maintain the blood at 37–38°C (Fig. 2). Venous blood drained from the lobe into a reservoir. Pump flow rate was set between 200 and 400 ml/min. The height of the reservoir was adjusted so that the venous pressure (Pv) was ~9 mmHg to maintain the lobes in zone 3 conditions when the airway pressure was 5 mmHg.

The lobe was ventilated with 6% CO2-17% O2-77% N2. Blood gases were sampled from the pulmonary venous line periodically and measured by using an Instrumentation Laboratories model 1304 analyzer. Sodium bicarbonate solution (1 meq/ml) was added to the venous reservoir as needed to neutralize metabolic acid. Average values were arterial PO2 of 112 ± 2 Torr, arterial PCO2 of 36 ± 1 Torr, and pH of 7.39 ± 0.01. There were no significant differences between blood gas measurements sampled at the beginning of the experiment and those sampled at the end (paired 2-tailed t-test, P > 0.10). A 100-ml tidal volume kept peak inspiratory pressure <10 mmHg. Expired pressure was set at 5 mmHg by a water overflow on the expiratory limb of the ventilator. Arterial pressure (Pa), Pv, and airway pressure were measured from

Fig. 1. A 3-capacitor-2-resistor (3C2R) compartmental model of pulmonary circulation. $F_T$, total flow into lung; $P_a$, pulmonary arterial pressure; $P_c$, pulmonary capillary pressure; $P_v$, pulmonary venous pressure; $C_1$, $C_2$, and $C_3$, compliances of arteries, capillaries, and veins, respectively; $R_1$ and $R_2$, resistance of arteries and veins, respectively, with any resistance in capillaries contributing equally to $R_1$ and $R_2$ (3).

Fig. 2. Schematic of experimental setup. ICCD, intensified charge-coupled device; A to D, analog-to-digital.
sideports in the respective cannulas (model P23 XL, Statham) zeroed at the level of the subpleural vessels under observation. The output from the pressure transducers was amplified (model 13-G4615–52, Gould), processed by a 50-Hz low-pass filter, then sampled at 100 Hz by an analog-to-digital board (model C10-DA508-PGA, Computer Boards) in a microcomputer (Dell 50-MHz 486).

**Video microscopy.** The lobe was suspended by two small spring-backed paper clips attached to opposite edges of the lobe (21) and raised until the uppermost pleural surface (the diaphragmatic surface in this orientation) came into contact with a transparent window. A 1.3-cm² area on the surface of the lobe was observed through the window. The windowpane was surrounded by a vacuum ring to prevent lateral movement of the observed area (20). Suspending the lobe against this manner allowed free downward expansion of the lobe during ventilation and prevented compression of the subpleural alveoli by the window. The remainder of the lobar surface was covered with a thin sheet of plastic to prevent drying and to slow the transpleural diffusion of gas.

The subpleural microcirculation under the window was observed with a modified Olympus BH2 reflectance microscope coupled to a Letz Ultrapak illuminator with x 11 objective. A fiber-optic light-guided illumination was obtained with a 200-W mercury arc lamp that was filtered with a combination of dichroic infrared-reflecting filters and broad-band-pass ultraviolet-absorbing filters to prevent tissue damage and a narrow band-pass interference filter to select the mercury green line (546 nm). Illumination for fluorescence microscopy was provided by a 100-W mercury arc mounted on the sidearm of the BH2 microscope, which was also filtered by dichroic infrared-reflecting filters and ultraviolet-absorbing filters. The light from this arc passed through a green band-pass exciter filter (500–560 nm) and a high-pass dichroic mirror (cutoff wavelength = 560 nm), which reflected the exciting light (mercury green line 546 nm) down through the objective onto the subpleural microcirculation beneath the window. Emitted light passed back through the objective, the dichroic mirror, and a red high-pass barrier filter (cutoff wavelength = 590 nm). Video recordings of the subpleural microcirculation were made with a Panasonic AG7050 SVS video recorder and a Cohu intensified charge-coupled device camera (model 5510), which was mounted on the microscope with a Nikon zoom CCTV adapter (model 79444).

**Vascular occlusions.** Arterial, venous, and double-occlusion maneuvers were performed in random order in each preparation with the lobe held in end expiration. Flow was occluded by stopcocks in the arterial inflow and venous outflow limbs of the perfusion circuit (Fig. 2). The stopcocks were controlled by actuators (cylinders containing a piston and rod), which closed the stopcocks when they were pressurized. Depending on the type of occlusion (arterial, venous, or double), one or both of the stopcocks were closed. Rotation of the stopcock valves interrupted flow without displacing volume from the site of occlusion. To perform an occlusion, a solenoid was energized, which pressurized the actuator(s) with compressed gas at 60 psi, closing the stopcock(s). The computer simultaneously marked time 0 in the pressure data file and activated a Panasonic WJ-810 time-date generator, which recorded elapsed time in milliseconds on the videotape. Arterial inflow to the lobe was constant during venous occlusion. Occlusions were performed in triplicate while a subpleural arteriole and venule observed with fluorescence microscopy were videotaped. The duration of each occlusion was ~3 s. Preclosure arteriolar and venular diameters were measured from the videotaped images as described previously (13).

For the off-line velocity measurements, the videotapes were replayed, and red blood cell velocities in subpleural precapillary arterioles and postcapillary venules were calculated by measuring the distance individual fluorescently labeled red blood cells moved from one video frame to the next. For each occlusion and in each vessel, one to three cells were counted in every video frame from 1 s before occlusion to 2 s after occlusion (90 video frames, 90–270 cells/occlusion). To reduce noise, a single velocity curve for each vessel for each type of occlusion was obtained by averaging the velocity curves from each of the triplicate occlusions for that set of conditions. The curves were averaged by computing the mean of the triplicate measurements at each point in time after occlusion. Similarly, a single average pressure decay curve was obtained for each type of occlusion on each lung lobe by averaging the pressure curves from the triplicate occlusions.

The measured response of the pressure-measuring system (transducer, amplifier, filter, and analog-to-digital board) to a square-wave pressure change from 20 mmHg to atmospheric pressure was >90% complete within 0.033 s or one video frame.

**Model-independent analysis.** The venous occlusion data were used to divide the total lobar vascular compliance into three compliances: one comprised of the compliance of arterioles >40 µm (Ca), another of vessels <40 µm (Cc), and a third of veins >40 µm in diameter (Cv). If the vascular bed is visualized as a longitudinally distributed distensible system, when the outflow is occluded while the inflow is maintained at a constant rate, the rate of change in pressure at all locations within the system will be equal and the axial flow observed at any site between the inlet and the site of occlusion will be the inflow rate minus the rate of volume storage in the distensible vessels upstream from the site of observation once the quasi-steady state has been established. The rate of upstream volume storage over the total flow will be the ratio of the upstream compliance to the total compliance. If the total compliance is estimated by measuring the change in pressure resulting from the total volume stored in the system up to a given time, the actual compliance of the segments upstream and downstream from the site of observation can be estimated. In the present study, two sites along the longitudinal distribution were available for observation on the subpleural surface: the ~40-µm arterioles and venules just upstream and downstream, respectively, from the capillary bed.

It is actually the volume flows, rather than the measured velocities, that are needed to estimate the compliance distribution. Because the vessels are distensible and the pressures are continuously increasing after venous occlusion, we converted the velocities to flows by using the following relationships

\[
v(t) = \frac{F(t)}{A(t)} = \frac{F(t)}{\pi \left( \frac{D(t)}{2} \right)^2}
\]

where \(v\), \(A\), \(D\), and \(F\) are the local velocity, vessel cross-sectional area (arterial or venous), diameter, and flow, respectively. Dividing the postocclusion (\(t > 0\)) velocity, \(v(t)\), by the preclosure velocity, \(v(0)\), gives

\[
\frac{v(t)}{v(0)} = \frac{F(t)}{F(0)} \frac{[D(0)]^2}{D(t)}
\]

Over the pressure range encompassed by the venous occlusion, 8.8–20 mmHg, \(D(t)\) can be related to \(D(0)\) by...
where \( \text{Pa}(t) = \frac{\text{Pav}(t) + \text{Pv}(t)}{2} \) and \( \alpha \) is the vessel distensibility, which was previously found for the lung preparation used in the present studies to be \( \sim 0.018/\text{mmHg} \) for the subpleural venules and \( 0.031/\text{mmHg} \) for the arterioles (14). Substituting Eq. 3 in Eq. 2 results in the following relationship between flow, velocity, and pressure

\[
\frac{F(t)}{F(0)} = \frac{\text{v}(t)[1 + \alpha \text{Pav}(t)]^2}{\text{v}(0)[1 + \alpha \text{Pav}(0)]} \quad (4)
\]

This relationship was used to convert the velocity measurements to flows, correcting for the pressure changes that occurred after venous, arterial, or double occlusion.

Because we could only measure the diameter of and the velocity in some individual vessels of the entire parallel set of \( \sim 40\mu\text{m} \) vessels, it was necessary to calculate fractional flows and, from them, fractional compliances. For each experiment, the flows between 0.5 and 2 s after occlusion were averaged, \( F_a \), and divided by the preocclusion flow rates averaged from \(-0.5 \) to \( 0 \) s, \( \text{F}(0) \), to obtain the normalized steady-state flow rates through the arteriole and venule \([\text{Fa}/\text{F}(0) \) and \( \text{Fv}/\text{Fv}(0) \), respectively]. The total compliance \( (C_T) \) was estimated as

\[
\text{C}_T = \text{Ca} + \text{Cc} + \text{Cv} = \frac{\text{FT}}{S} \quad (5)
\]

where \( S \) is the slope of \( \text{Pv}(t) \) obtained by linear regression over the time interval \( 0.5-1.0 \text{ s} \) after venous occlusion and \( \text{FT} \) is the lobar inflow rate. Before venous occlusion, the flow through 40-\( \mu \text{m} \) arterioles (\( \text{Fa} \)) and venules (\( \text{Fv} \)) is equal to the total lobar flow rate

\[
\text{Fa}(0) = \text{Fv}(0) = \text{FT} = \text{C}TS \quad (6)
\]

After venous occlusion, after the quasi-steady state is reached, the flow rate through the arterioles is equal to the total flow rate minus the volume stored in upstream vessels

\[
\text{Fa}(t) = \text{FT} - \text{CaS} \quad (7)
\]

Solving Eq. 5 for \( \text{FT} \) and substituting for \( \text{FT} \) in Eq. 7 gives

\[
\text{Fa}(t) = (\text{Ca} + \text{Cc} + \text{Cv})S - \text{CaS} = (\text{Cc} + \text{Cv})S \quad (8)
\]

Similarly, the flow rate through the venules after venous occlusion is equal to the total flow rate minus the volume stored in upstream vessels

\[
\text{Fv}(t) = \text{FT} - (\text{Ca} + \text{Cc})S = \text{ CvS} \quad (9)
\]

During the quasi-steady state, \( \text{Fa}(t) = \text{Fa} \) and \( \text{Fv}(t) = \text{Fv} \). Therefore, dividing Eq. 8 by Eq. 6 gives the fractional compliance downstream from the arteriolar measurement site

\[
\frac{\text{Fa}(t)}{\text{Fa}(0)} = \frac{\text{Cc} + \text{Cv}}{\text{C}_T} \quad (10)
\]

and dividing Eq. 9 by Eq. 6 gives the fractional compliance downstream from the venular measurement site

\[
\frac{\text{Fv}(t)}{\text{Fv}(0)} = \frac{\text{Cv}}{\text{C}_T} \quad (11)
\]

The occlusion time intercepts, \( \text{Pa}_i \) and \( \text{Pv}_i \), of the simultaneously measured \( \text{Pa} \) and \( \text{Pv} \) after venous occlusion were obtained by linear regression of \( \text{Pa}(t) \) and \( \text{Pv}(t) \) over the time interval \( 0.5-1.0 \text{ s} \). These intercepts were used along with the compliances to put bounds on the resistances upstream from, between, and downstream from the 40-\( \mu \text{m} \) arterioles and venules, as previously described (3, 4, 7).

Model-dependent analysis. The above calculations are model independent, in that no specific compartmental arrangement of resistances and compliances is assumed. In addition, they utilize only the quasi-steady-state flow and pressure data from the venous-occlusion maneuver. Compartimental model representations can also be used to interpret the transient portions of the postocclusion data. Audi et al. (1, 2) provided the rationale for using a 3C2R model representation of the lobar vasculature for interpreting the occlusion pressure data (Fig. 1). Conceptually, the upstream resistance \( (R_1) \) was visualized as representing primarily the resistance of the small arteries, and the downstream resistance \( (R_2) \) was visualized as primarily the resistance of the small veins, with any capillary resistance contributing approximately equally to both \( R_1 \) and \( R_2 \) (Fig. 1). By use of the anatomically defined compliances from the arteriolar and venular flow measurements (\( \text{Ca}, \text{Cc}, \text{ and } \text{Cv} \)) as model inputs for the upstream (\( \text{C}_1 \)), middle (\( \text{C}_2 \)), and downstream (\( \text{C}_3 \)) compliances, respectively, the 3C2R model resistances were calculated (16) by using the double-occlusion pressure (\( \text{Pd} \))

\[
R_2 = \frac{[\text{Pd} - \text{Pv}(0)]C_T - [\text{Pa}(0) - \text{Pv}(0)]C_1}{C_T C_2} \quad (12)
\]

and

\[
R_1 + R_2 = \frac{\text{Pa}(0) - \text{Pv}(0)}{\text{FT}} \quad (13)
\]

where \( \text{Pa}(0) \) and \( \text{Pv}(0) \) are the preocclusion steady-state \( \text{Pa} \) and \( \text{Pv} \), respectively. The 3 C's used as model inputs were obtained by first estimating \( \text{C}_T \) from the average pressure data by using Eq. 5. The values of \( \text{C}_1, \text{C}_2, \text{ and } \text{C}_3 \) were then calculated as the products of the fractional compliances and \( \text{C}_T \) (Table 1). Once the model resistances were calculated, we investigated to what extent the arteriolar and venular flows measured during venous, arterial, and double occlusions were consistent with the compliances and model resistances derived from the venous occlusion flows and double-occlusion pressure. This was accomplished by numerically solving the following governing differential equations for the 3C2R model (16) describing the time variations in \( \text{Pa}(t), \text{Pc}(t) \), and \( \text{Pv}(t) \)

\[
\frac{d\text{Pa}}{dt} = \frac{\text{FT} - \left( \frac{\text{Pa} - \text{Pc}}{R_1} \right)}{C_1} \quad (14)
\]

\[
\frac{d\text{Pc}}{dt} = \frac{(\text{Pa} - \text{Pc})}{R_1} - \left( \frac{\text{Pc} - \text{Pv}}{R_2} \right) \quad (15)
\]

\[
\frac{d\text{Pv}}{dt} = \left( \frac{\text{Pc} - \text{Pv}}{R_2} \right) - \text{F}_{\text{res}} \quad (16)
\]

with the initial \(( t = 0 \) conditions \( \text{Pa}(0) = \text{Pv}(0) + \text{FT}(R_1 + R_2) \) and \( \text{Pc}(0) = \text{Pv}(0) + \text{FT}R_2 \), where \( \text{F}_{\text{res}} \) is the flow into the reservoir.

Equations 14–16 were solved numerically for \( \text{Pa}(t), \text{Pc}(t) \), and \( \text{Pv}(t) \) after \( \text{F}_{\text{res}} \) was set to 0 for venous occlusion and \( \text{FT} = \text{F}_{\text{res}} = 0 \) for double occlusion. For arterial occlusion, \( \text{FT} \) was set
and only Eqs. 14 and 15 were solved for Pa(t) and Pc(t), with Pv(t) set equal to the measured postocclusion venous pressure. These pressures were then used to calculate the postocclusion arteriolar and venular flows

\[ F_a(t) = \frac{Pa(t) - Pc(t)}{R_1} \]  
\[ F_v(t) = \frac{Pc(t) - Pv(t)}{R_2} \]

RESULTS

Direct measurements. The normalized arteriolar and venular velocities from the individual experiments measured during the occlusion maneuvers are presented in Figs. 3–5. The averages of the pressure curves obtained during the occlusion maneuvers are shown in Fig. 6. The mean values of the various measurements obtained during the preocclusion period or from the quasi-steady states during venous or double occlusion are summarized in Table 1.

Model-independent analysis. To carry out the analysis of these measurements, the velocities were converted to normalized flows (Fig. 7) using Eq. 4. The fractional compliances estimated from these flows (Eqs. 10 and 11) are shown in Table 2. The Cc fraction was significantly larger than either Ca or Cv (P < 0.01, analysis of variance followed by Newman-Keuls test). The upper and lower bounds placed on the resistances partitioned by the 40-µm arterioles and venules are also shown in Table 2.

Model-dependent analysis. When the 3C2R model and Pd were used to interpret the data, R1/RT was nearly equal to R2/RT (Table 3). The simulated venous and double-occlusion pressure curves, generated by solving Eqs. 14–16 for Pa(t) and Pv(t), and the simulated arterial-occlusion pressure curves, generated by solving Eqs. 14 and 15 for Pa(t), are shown in Fig. 8.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pa (0)</td>
<td>Preocclusion lobar arterial pressure</td>
<td>13.1 ± 0.6 mmHg</td>
</tr>
<tr>
<td>Pv (0)</td>
<td>Preocclusion lobar venous pressure</td>
<td>8.9 ± 0.5 mmHg</td>
</tr>
<tr>
<td>Paw</td>
<td>Lobar airway pressure</td>
<td>5.0 ± 0.0 mmHg</td>
</tr>
<tr>
<td>Ct</td>
<td>Total pulmonary vascular compliance</td>
<td>1.29 ± 0.10 ml/mmHg</td>
</tr>
<tr>
<td>R1</td>
<td>Total pulmonary vascular resistance</td>
<td>0.88 ± 0.18 mmHg·s·ml⁻¹</td>
</tr>
<tr>
<td>Ft</td>
<td>Total lobar mean flow</td>
<td>5.28 ± 0.51 ml/s</td>
</tr>
<tr>
<td>Pa0</td>
<td>Zero intercept of Pa(t) after VO</td>
<td>13.0 ± 0.6 mmHg</td>
</tr>
<tr>
<td>Pvo</td>
<td>Zero intercept of Pv(t) after VO</td>
<td>10.4 ± 0.4 mmHg</td>
</tr>
<tr>
<td>Dv (0)</td>
<td>Preocclusion venular diameter</td>
<td>41.7 ± 2.6 µm</td>
</tr>
<tr>
<td>vvo (0)</td>
<td>Preocclusion venular velocity</td>
<td>692 ± 63 µm/s</td>
</tr>
<tr>
<td>vvo (0)</td>
<td>Preocclusion venular velocity</td>
<td>707 ± 64 µm/s</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 6 vessels. VO, venous occlusion.

Fig. 3. Red blood cell velocities, v(t), before and after venous occlusion as a fraction of their mean velocity during preocclusion measurement period, v(0). Lines, measurements from a single 40-µm arteriole (A) and venule (B) in each of 6 lobes. Time 0 (vertical dashed line) is time of occlusion. Filled bar on x-axis represents quasi-steady-state data used to calculate compliance.

Fig. 4. Red blood cell velocities, v(t), before and after arterial occlusion as a fraction of their mean velocity during preocclusion measurement period, v(0). Lines, measurements from a single 40-µm arteriole (A) and venule (B) in each of 6 lobes. Time 0 (vertical dashed line) is time of occlusion.
The arteriolar and venular flows predicted by Eqs. 17
and 18 after arterial and double occlusion followed the
trend in the measured flows to the extent shown in
Figs. 9 and 10.

DISCUSSION

The key observation in this study was a large de-
crease in venular flow, but only a small fall in arteriolar
flow, after venous occlusion. Thus, after occlusion, a
relatively small fraction of the flow continued into veins
40 µm and a relatively small fraction was diverted
into distending arteries 40 µm. The largest fraction,
65% of the flow, increased the volume of vessels
<40 µm, presumably mostly capillaries. Therefore, the
capillaries contained the largest fraction of lobar vascu-
lar compliance. The relatively rapid fall in arteriolar
flow in comparison to venular flow after arterial occlu-
sion indicates that the time constant for emptying
vessels upstream from the 40-µm arterioles was small
in comparison to that upstream from the 40-µm ven-
ules, again consistent with a relatively small fraction of
the compliance in the arteries compared with the
capillaries. Unlike previous occlusion studies, our video-
microscopic observations were made at specific ana-
tomic locations (40-µm-diameter arterioles and venu-
es), which allowed us to partition compliance into
anatomically defined segments.

Relative arterial-capillary-venous distribution of
compliance implied by these results of 8:65:27 can be
compared with compliance distributions obtained for
the intrapulmonary vessels of the lungs by other meth-
ods, which include 30:49:21 for the dog lung lobe

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractional compliance in arteries &gt;40 µm (Ca/Cr)</td>
<td>0.08 ± 0.06</td>
</tr>
<tr>
<td>Fractional compliance in vessels &lt;40 µm (Cc/Cr)</td>
<td>0.65 ± 0.07</td>
</tr>
<tr>
<td>Fractional compliance in veins &gt;40 µm (Cv/Cr)</td>
<td>0.27 ± 0.04</td>
</tr>
<tr>
<td>Fractional resistance in arteries &gt;40 µm</td>
<td>0.64–0.13</td>
</tr>
<tr>
<td>Fractional resistance in vessels &lt;40 µm</td>
<td>0.51–0.09</td>
</tr>
<tr>
<td>Fractional resistance in veins &gt;40 µm</td>
<td>0.45–0.26</td>
</tr>
</tbody>
</table>

Compliance values are means ± SE; n = 6 vessels. Resistance
values are upper and lower bounds calculated according to Eq. 3. Ca,
arterial compliance; Cv, compliance of veins; Cc, compliance of
vessels <40 µm.
vascular bed (7) and 7:79:14 for the whole dog lung vascular bed (5). Consistent with previous studies, the results of the present study lead to the conclusion that the arteries and veins account for smaller fractions of the total intrapulmonary vascular compliance than the capillaries. Thus the results further support the concept that the intrapulmonary vascular compliance is concentrated in the capillary bed.

The compliances estimated from the venous occlusion flows are based on the concept that the fractional changes in flows in the subpleural vessels are close to those in similarly sized vessels in the interior of the lungs. This is a difficult assumption to test directly. It is conceivable that at least one reason for any differences between these estimates for arterial, capillary, and venous compliances based on the subpleural vessel flows and those estimated by other means, for what might be assumed to be the same vascular segments (5, 7), might be the result of deviations from this assumption. However, the basic agreement between the results of this study and those obtained by very different methods (5, 7) supports the concept that the surface arterioles and venules reflect the behavior of the internal vessels. Also supporting this concept, Short et al. (17) found that recruitment of subpleural capillaries in the rat lung paralleled recruitment of interior capillaries over a range of pressures that spanned low zone 3 to high zone 1. Finally, Hillier et al. (15), using fluorescent microspheres, found no redistribution of flow between subpleural and interior vessels in the isolated canine lobe during airway hypoxia. Although these studies do not directly compare subpleural with interior flow changes after vessel occlusion, they demonstrate that subpleural perfusion parallels interior perfusion over a wide range of hemodynamic conditions.

We divided total pulmonary vascular compliance into three segments bounded by 40-µm arterioles and venules, because one cannot assume that compliance is evenly distributed over the entire diameter range, these bounds do not tell us anything about the distribution of compliance within

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractional resistance upstream from vessels &lt;40 µm (R1/RT)</td>
<td>0.47 ± 0.07</td>
</tr>
<tr>
<td>Fractional resistance downstream from vessels &lt;40 µm (R2/RT)</td>
<td>0.53 ± 0.07</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 6 vessels. R1, upstream resistance; R2, downstream resistance.

![Fig. 8. Arterial pressure, Pa, and venous pressure, Pv, before and after arterial, venous, and double occlusion. Thick lines, pressures predicted by 3C2R model using model parameters estimated as indicated in text; thin lines, average of actual mean pressure curves from each of 6 lobes as shown in Fig. 5. Filled bar on x-axis represents quasi-steady-state data used to calculate compliance.](http://jap.physiology.org/cgi/content/fig/9/2/309)

Fig. 9. Calculated flow rates, F(t), before and after arterial occlusion as a fraction of mean flow rate during preocclusion measurement period, F(0). Flows were calculated from red blood cell velocities through ~40-µm subpleural arterioles (thin solid lines) and ~40-µm subpleural venules (thin dotted lines). A single arteriole and a single venule were measured in each of 6 lobes. Thick lines, 3C2R predictions for flows through resistances upstream and downstream from C2, with R and C values estimated from venous and double occlusions. Time 0 (vertical dashed line) is time of occlusion.

![Fig. 10. Calculated flow rates, F(t), before and after double occlusion as a fraction of mean flow rate during preocclusion measurement period, F(0). Flows were calculated from red blood cell velocities through ~40-µm subpleural arterioles (thin solid lines) and ~40-µm subpleural venules (thin dotted lines). A single arteriole and a single venule were measured in each of 6 lobes. Thick lines, 3C2R predictions for flows through resistances upstream and downstream from C2, with R and C values estimated from venous and double occlusions. Time 0 (vertical dashed line) is time of occlusion.](http://jap.physiology.org/cgi/content/fig/9/2/309)
these three segments. Instead, the sites where the measurements were made put lower bounds on the diameter of arteries and veins contributing to the compliance of the upstream and downstream segments, respectively. Likewise, the measurement sites put upper bounds on the size of vessels contributing to the compliance of the middle segment. Nevertheless, the available anatomic evidence (8) suggests that there is little volume and, therefore, little compliance in noncapillary vessels <40 µm. Most of the compliance in the middle segment, therefore, is probably in the capillaries.

If the pressure data are included in the analysis, the occlusion maneuvers also provide information about how resistance is distributed with respect to compliance. The bounds placed on resistance associated with each of the three compliances using the quasi-steady-state data, i.e., the model-independent interpretation, are rather wide. The most important conclusion from these bounds is that no more than ~50% of the total resistance is associated with vessels <40 µm. If, instead, the 3C2R model is used to interpret the data, the two resistances, R1 and R2, are nearly equal under the conditions of this study. Like the finding that the major locus of compliance is in the capillaries, this distribution of resistance is consistent with previous interpretations. The bounds placed on resistance associated with vessels in the middle segment, therefore, is probably in the capillaries.

In summary, we have obtained anatomic data on microvascular flow changes in vivo in dog lung lobe. These compliance measurements, when combined with the 3C2R model (2) and flow measurements after occlusion of arterial inflow and simultaneous occlusion of arterial inflow and venous outflow, suggest that most of the compliance in arteries of >40 µm is upstream from any resistance in these vessels and the compliance in veins of >40 µm is downstream from any resistance in these vessels.

The authors thank Dr. Tawfik S. Hakim for assistance with pilot studies. This work was supported by National Heart, Lung, and Blood Institute Grants HL-36033 and HL-19298 and the Department of Veterans Affairs.