Noninvasive Estimation of Pulmonary Arterial Pressure by Analysis of Pulmonary Blood-Flow Distribution

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To determine whether a correlation exists between pulmonary arterial (PA) pressure (P_a) and the distribution of pulmonary blood flow, this distribution was measured in four upright dogs in the control state and during intravenous infusions of epinephrine or prostaglandin $F_{2\alpha}$. During suspension of respiration, 15 mCi of Xe-133 were injected intravenously, and perfusion and equilibration lung images were recorded with a scintillation camera. The procedure was performed several times on each dog, with and without pharmacological elevation of PA pressure by 5 to 50 cm H_2O. For each scintigram, the relative blood flow per unit ventilated lung volume (F) was plotted against centimeters above the hilum (h). Pulmonary arterial pressure was derived from each curve, assuming the relation $F = B(P_a - hD)^2$, where B = constant and D = specific gravity of blood. Calculated PA pressure correlated strongly (r = 0.83) with measured PA pressure, suggesting a possible means of noninvasive estimation of PA pressure.

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Previous work has demonstrated relationships between the distribution of blood flow in the lungs and both pulmonary venous (PV) and pulmonary arterial (PA) pressures (*1–11*). Although a correlation has been found between PA pressure and the ratio between the flow rates in upper and lower lung zones (U/L) in upright subjects, (*2–5,7,8*) some studies have shown that U/L correlates best with pulmonary capillary wedge pressure (*5,8*). In addition, U/L has been correlated with cardiac output (*4,5,8*), pulmonary vascular resistance (*2–5,7*), and cardio–thoracic ratio (*4,5*).

Pulmonary blood-flow distribution is a complex function. At least three zones of the upright lung have been defined (*9,11,12*), and in each zone blood flow depends in a different way on PA pressure, pulmonary venous (PV) pressure, alveolar pressure (P_{alv}), pulmonary vascular resistance, and the effect of gravity (Fig. 1). It would be surprising if a single measurement such as U/L consistently correlated with any one hemodynamic parameter. In the present study we analyzed the blood-flow distribution in the upper lung zone of upright animals in the control state and following pharmacological elevation of PA pressure, in order to determine whether this blood-flow distribution could be used to indicate PA pressure.

MATERIALS AND METHODS

Four dogs were anesthetized with pentobarbital, intubated, and ventilated at constant tidal volume and rate with a Harvard pump respirator. The dogs

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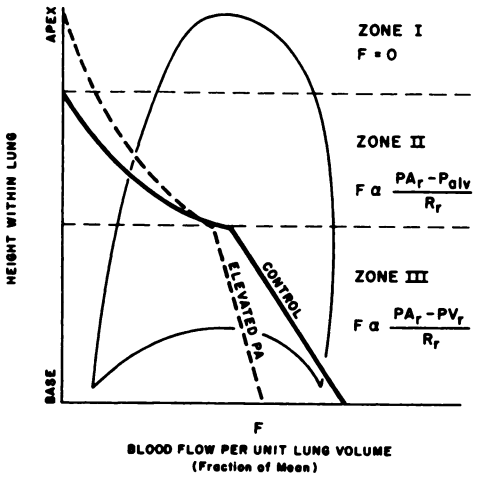

FIG. 1. Diagram depicting distribution of blood flow in an upright lung. When PA pressure is raised, blood flow becomes more uniform (see Discussion section). Division drawn between zone I and zone II relates to control curve. PA_r = regional PA pressure; PV_r = regional PV pressure; R_r regional resistance to blood flow.

were placed upright in front of an Anger scintillation camera equipped with an all-purpose, parallel-hole, low-energy collimator. The scintillation camera was interfaced to a dedicated nuclear medicine computer system with a matrix resolution of 5 mm per pixel. Pulmonary arterial pressure and cardiac output were monitored with a Swan–Ganz thermodilution catheter attached to a Statham strain gauge with amplifier†, recorder, and a thermodilution cardiac-output computer‡. The catheter entered a femoral vein and was positioned under fluoroscopic observation in a central pulmonary artery. The location of the catheter in the hilum was recorded by imaging after the instillation of 0.5 mCi of xenon-133 in saline into the balloon. This location was taken as the reference level for PA pressure measurement. An image of two cobalt-57 markers, placed exactly 5 cm apart, was used to calibrate the pixel size. Airway pressure was monitored with an in-line pressure gauge.

PROCEDURE

During suspension of respiration at end-expiration (P_{alv} = 0), 15 mCi of xenon-133 were injected intravenously and a 30-sec anterior lung perfusion image was recorded using a 20% window over the 80-keV photopeak. Ten milliliters of saline at 4°C were injected through the proximal lumen of the Swan–Ganz, and cardiac output was determined. After 1 min of rebreathing, a 30-sec equilibration image was obtained to provide a distribution of the ventilated air space. Following a 15-min period of xenon clearance, a 30-sec background image was recorded, and epinephrine or prostaglandin $F_{2\alpha}$‖ ($PGF_{2\alpha}$) was infused intravenously at a rate sufficient to increase PA pressure by 5 to 50 cm H_2O, at which time the xenon injection, imaging, and cardiac output measurements were repeated. The procedure was repeated four to six times in each dog, with and without epinephrine or $PGF_{2\alpha}$ infused intravenously at several different rates.

DATA ANALYSIS

Each perfusion and equilibration image was normalized for total counts and corrected for xenon background by subtracting the background image. A vertical slice profile of each scintigram was then generated by the computer system. The number of counts in each 5-mm-high zone (one picture element) of the perfusion image from apex to base was divided by the number of counts in the corresponding zone of the equilibration image, yielding the relationship of relative blood flow per unit ventilated lung volume (F) to distance above the hilum (h). $F = \dot{Q}_r/\dot{Q}_m$, where $\dot{Q}_r$ = regional blood flow per unit ventilated lung volume, and $\dot{Q}_m$ = mean blood flow per unit ventilated lung volume for the whole lung.

Postulated relation between PA pressure (P_a) and pulmonary blood-flow distribution. In the upper zone of the lung,

$$\dot{Q}_r \propto (P_a - hD - P_{alv})/R_r,$$

where P_a and P_{alv} are expressed in cm of H_2O, h is in cm, D = specific gravity of blood = 1.06, and R_r = regional resistance to blood flow (*9,11,12*). Since pulmonary vessels are distensible, R_r is inversely related to perfusion pressure, $P_a - hD$ (*9,12*). The simplest assumption is that

$R_r \propto 1/(P_a - hD)$, in which case

$\dot{Q}_r \propto (P_a - hD - P_{alv}) \times (P_a - hD)$, and

$$F = \dot{Q}_r/\dot{Q}_m = B(P_a - hD - P_{alv}) \times (P_a - hD),$$

where B is a constant, inversely proportional to $\dot{Q}_m$. Since during our measurements, P_{alv} = 0,

$$F = B(P_a - hD)^2 \quad (1)$$

For each plot of F against h, points corresponding to the region between the apex and 4 cm below the apex were selected, and these points were fitted to Eq. 1, permitting calculation of P_a by least-square analysis. No point chosen contained less than four times background counts. Using least-squares linear regression, comparisons were made between calculated and measured values of P_a, and between calculated P_a and measured cardiac output.

RESULTS

Using infusions of epinephrine or $PGF_{2\alpha}$, mean

TABLE 1. EFFECTS OF EPINEPHRINE AND PROSTAGLANDIN $F_{2\alpha}$ ON PA PRESSURE (P_a) AND CARDIAC OUTPUT (CO)

	Baseline (N = 6)		Epinephrine (N = 10)		Prostaglandin $F_{2\alpha}$ (N = 5)	
	P_a*	CO†	P_a	CO	P_a	CO
Mean	12.5	2.5	31.4	3.4	24	2.1
s.e.m.‡	2.0	0.45	4.5	0.54	4.7	0.37

* cm H_2O.
† Liters per min.
‡ Standard error of the mean.

PA pressure was varied between 7 and 62 cm H_2O, with epinephrine tending to increase and $PGF_{2\alpha}$ tending to decrease cardiac output (Table 1). In each dog, as PA pressure was raised, the distribution of pulmonary blood flow tended to appear more uniform, as is evident on the perfusion lung images and on plots of F against h (Fig. 2). When PA pressure was calculated using points corresponding to the upper lung zones, fitted to Eq. 1, a strong correlation was found between estimated and measured values of mean PA pressure ($r = 0.83$, $p < 0.0001$; Fig. 3). There was no significant correlation between calculated PA pressure and cardiac output ($r = -0.195$, $p = 0.40$; Fig. 4).

DISCUSSION

West et al. have defined three zones in the upright isolated dog lung (*9,11,12*) (Fig. 1). At the lung base (zone III), regional blood flow is dependent on (regional PA pressure − regional PV pressure)/regional resistance to blood flow (R_r). Although the difference between regional PA pressure and regional PV pressure remains constant throughout zone III, blood flow diminishes from base toward apex because the gravitational decreases in regional PA pressure and regional PV pressure reduce vascular distension, resulting in a rise in R_r. Closer to the apex (zone II), P_{alv} exceeds regional PV pressure, and regional blood flow is dependent on (regional PA pressure − P_{alv})/R_r. Here blood flow decreases more rapidly toward the apex than in zone III, since in zone II regional PA pressure minus P_{alv} falls, and R_r rises toward the apex. If a high enough point is reached, such that regional PA pressure falls below P_{alv}, blood flow ceases (zone I).

When PA pressure is raised, the distribution of pulmonary blood flow changes (*9,11,12*). At a higher PA pressure, any gravitational fall in perfusion pressure represents a smaller fraction of PA pressure. Therefore, at an elevated PA pressure, the fall in regional blood flow with any given rise in lung height represents a smaller fraction of mean blood flow. Furthermore, as PA pressure rises, the transition point between zone I and zone II (i.e., the height of the lung at which blood flow stops) rises toward or above the apex. If the relationship between PA pressure, lung height, and relative regional blood flow (regional blood flow expressed as a fraction of mean blood flow) were known, then PA pressure could be calculated from the curve of relative regional blood flow plotted against lung height in zone II.

We based our calculations of PA pressure on points from the apical 4 cm of each relative blood-

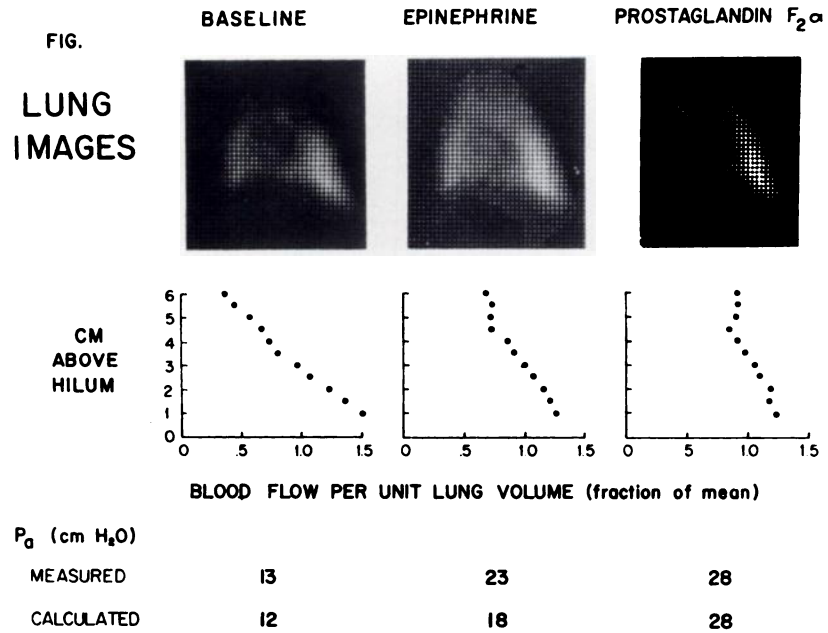

FIG. 2. Xenon-133 images and corresponding perfusion curves. PA pressure was raised above baseline by i.v. infusion of epinephrine and prostaglandin $F_{2\alpha}$.

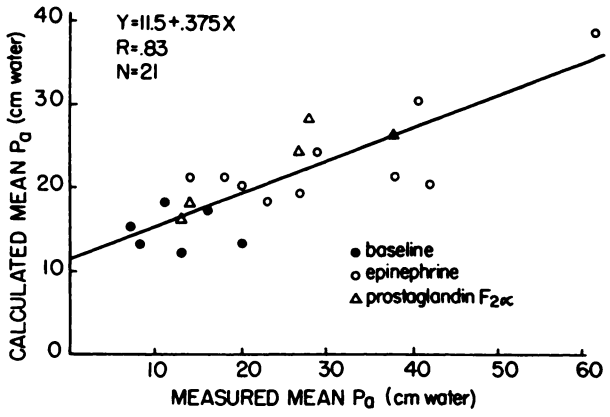

FIG. 3. Graph demonstrating correlation between measured and calculated values of PA pressure.

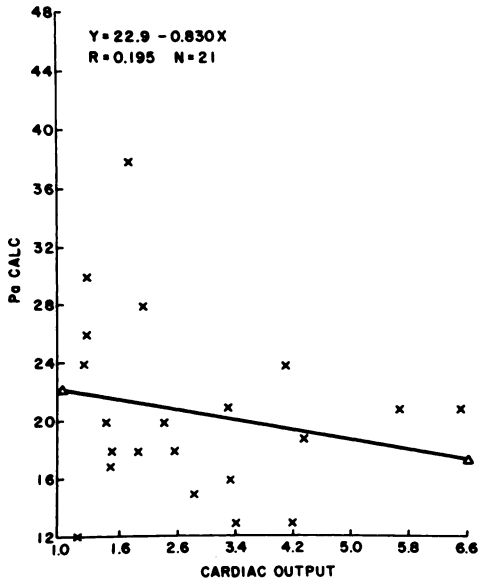

FIG. 4. Graph relating cardiac output (liters per min) and calculated PA pressure (cm H_2O). Correlation is not significant.

flow curve fitted to Eq. 1:

$$F = B(P_a - hD)^2.$$

This equation was based on two assumptions concerning regional blood flow in zone II: a) that relative regional blood flow per unit ventilated lung volume is directly proportional to (regional PA pressure − P_{alv})/regional resistance, and b) that regional resistance is inversely proportional to regional PA pressure. On the basis of the current data we cannot be certain that the latter assumption is the best one possible. Nevertheless, a strong correlation was found between calculated and measured values of PA pressure.

One implication of Eq. 1 is that PA pressure is related to the height at which blood flow ceases, i.e., where F = 0, P_a = hD. In other words, flow stops when hilar PA pressure is balanced by the pressure exerted by a vertical column of blood above the hilum. This pressure, measured in centimeters of H_2O, equals the height in centimeters of the column (h), times the specific gravity of blood (D).

Using epinephrine and $PGF_{2\alpha}$, we raised PA pressure by two different mechanisms. Elevation of PA pressure due to epinephrine resulted primarily from its positive inotropic and chronotropic actions (*13*), as evidenced by an increase in cardiac output, whereas pulmonary vasoconstriction was minimal. $PGF_{2\alpha}$ raised PA pressure predominantly by pulmonary vasoconstriction (*14,15*). Positive inotropic and chronotropic actions were less important, and cardiac output fell or remained unchanged. The effects of these two drugs on the distribution of pulmonary blood flow were similar, and the correlation between calculated PA pressure and cardiac output was not significant.

Ball et al. originally developed a technique by which xenon-133, detected with individual scintillation counters, could be used to measure relative pulmonary blood flow per unit ventilated lung volume in three different zones of the upright lung (*1*). Since that time, several clinical investigations have been performed, correlating hemodynamic measurements with pulmonary blood-flow distribution, using either xenon-133 (*2,6*) or radionuclide-labeled particles (*3–5,7,8*). Most of these studies were done in patients with mitral stenosis, correlating U/L, the ratio between the flow rates in the upper and lower lung zones, with pulmonary capillary wedge pressures. West, Dawson, and others have postulated that elevation of PV pressure results in transudation of fluid into the perivascular interstitial space in the dependent zones of the lung, and that vascular resistance in these zones rises accordingly (*2,6,10, 12*). The effect is a decrease in lower-zone blood flow and reversal of the usual upper- to lower-zone flow ratio—namely, U/L increases. However, pulmonary arterial hypertension can similarly alter U/L, since, as explained above, when PA pressure is increased, relative regional blood flow drops more slowly from base toward apex (*9,11,12*). Although U/L appears to correlate best with pulmonary capillary wedge pressure (*5,8*), at least some of its variability has been ascribed to differences in PA pressure (*2–5,7,8*). Because of the dependence of U/L on multiple factors, enthusiasm regarding the clinical usefulness of this measurement has been variable.

The present study suggests that analysis of the distribution of upper-zone pulmonary blood flow may be useful in estimating PA pressure. Before

our findings can be applied clinically, however, two reservations must be stated. First, our assumptions regarding the relationship between regional blood flow, lung height, and PA pressure apply only to zone II, in which regional blood flow depends on regional PA pressure minus P_{alv}. In a patient with an elevated PV pressure, regional PV pressure may exceed P_{alv} throughout the lung (i.e., zone III conditions), and regional blood flow would then depend on regional PA pressure minus regional PV pressure, even at the apex. In this situation, which could be recognized from the contour of the flow distribution curve, it may be difficult or impossible to estimate PA pressure accurately from the pulmonary blood-flow distribution. Second, it is unlikely that PA pressure can be inferred from the pulmonary blood-flow distribution in patients in whom the pattern of blood flow is markedly disturbed by severe parenchymal lung disease. These reservations considered, further studies are warranted to assess the applicability of our findings to the clinical setting.

FOOTNOTES

† Harvard Instrument Co., Massachusetts.
‡ International Laboratories, Waterville, MA.
‖ Upjohn Company, Kalamazoo, MI.

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