The physical properties of human pulmonary arteries and veins


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Summary

1. We have studied the extensibility of circumferential strips of main pulmonary artery and large pulmonary veins obtained at post mortem from patients of all ages, dying from conditions other than heart and lung disease.

2. The vessel strips were submitted to increasing loads in a tension balance. The pulmonary arteries were found to be readily extensible. This extensibility became less with increasing age. The pulmonary veins were virtually inextensible at all ages.

3. It is postulated that the large extraparenchymal pulmonary veins have a capacitative role in supplying blood from the lungs to the left atrium. This may be accomplished by their collapsible nature, as they have little capability of distension.

Key words: lung, pulmonary vessels.

Introduction

Normal lung capillary blood flow in man is pulsatile (Lee & Du Bois, 1955; Bosman, Honour, Lee, Marshall & Scott, 1964). Even in patients with cardiopulmonary disease leading to pulmonary hypertension this pulsatility is preserved (Karatzas & Lee, 1970). The capillary blood flow pulse closely resembles the pressure wave from the pulmonary artery, though delayed somewhat in time.

We have previously shown how the arterial system adapts to preserve the input characteristics of the lung capillary bed unchanged so that the pulsatile form of lung capillary blood flow is unaffected by changes in pulmonary arterial resistance (Reuben, Gersh, Swadling & Lee, 1970; Reuben, Swadling, Gersh & Lee, 1971; Reuben, 1970, 1971; Lee, 1971), with a simple hyperbolic relationship between pulmonary arterial resistance, responsible for the pulmonary hypertension and pulmonary arterial compliance, as the rising pulmonary arterial pressure distends the pulmonary arterial system.

The way in which the pulmonary venous system isolates the lung capillaries from pressure changes in the left heart is much less well understood. For, although the pulmonary venous system is not equipped with valves, the profile of capillary blood flow is normally entirely unaffected by the pressure events taking place in the left atrium throughout the cardiac cycle (Karatzas & Lee, 1970; Gillespie, Green, Karatzas & Lee, 1967). This implies that the lung venous system damps out retrograde pressure pulsations originating in the left atrium. This could arise if the pulmonary veins were very distensible structures. Harris, Heath & Apostolopoulos (1965) examined the extensibility of the human pulmonary arterial trunk and compared it with that of the aorta, but they did not study pulmonary veins. We have now studied the pulmonary veins by similar methods.
Methods

Stress-strain measurements were made on post-mortem specimens taken from the main branches of the pulmonary artery and from the largest pulmonary vein lying outside the lung parenchyma, and at least 0.5 cm from the left atrium, in 112 patients aged 7-87 years, who had died from causes other than heart or lung disease. The vessels were cut away from the heart and lungs, any attached loose adventitious materials being removed. The vessels were opened along their longitudinal axis and laid flat upon the bed of a specially constructed guillotine, which punched out a 2.5 cm × 1.0 cm circumferential strip of vessel. The strips of pulmonary artery and pulmonary vein were then weighed.

The vessels were stored in Krebs-Ringer solution and immediately studied, mounted in a tension balance as described by Harris et al. (1965). Each strip was first attached to the uppermost clamp of the tension balance (A, Fig. 1), so as to hang between the jaws of the lower clamp A', which was fixed to an adjustable mounting frame (B, C, D) within a Perspex chamber.

Fig. 1. Diagram of tension balance. The vessel strip to be tested is suspended between fixed and mobile clamps (A–A') immersed in Krebs–Ringer solution within a Perspex container (C). The mobile clamp attached to the vessel is connected via a thread and pulley to a cantilever balance. Vessel length-tension measurements, at different loads, are made by means of the screw mechanism (B–D), which enables the position of the fixed clamp to be altered. See the Methods section.

The jaws of the lower clamp of the apparatus were then closed, the balance arm of the apparatus (E, F) registering zero tension as the vessel strip was attached. The distance between the clamps A–A' was then measured by a travelling microscope. The Perspex chamber was then filled with Krebs–Ringer solution and the mounting frame (B, C, D) reset so that the tension balance (E, F) again registered zero. The vertical cut edges of the vessel strip between the clamps A–A' never appeared absolutely straight, suggesting that the strip hung slackly when in the solution. Increases in strip length with test loads were thus due to removal of this slack, but this could not be prevented. However, with zero load the vessel strip resumed its original configuration, so that an arbitrary ‘zero load length’ was therefore chosen as the length of vessel strip when the load was 1 g. This was the minimum load required to remove any visible slack in the vessel strip when mounted in Krebs–Ringer solution as above. Apter (1966) also found that the load required to unbend aortic rings without stretch varied from 2 to 7 g. After 5 min to allow for ‘creep’ to occur within the vessel strip, tissue-length measurements were always stable. Tissue length was then measured with increasing loads, with a final reading at the original ‘zero load’ of 1 g. Any strips which showed a persistent increase in this final length at 1 g load of more than 1% for veins and 5% for arteries was discarded. We studied strips from 85 pulmonary veins and 62 pulmonary arteries which met these criteria.

After the tension-balance studies the strips were fixed in 10% neutral formol/saline at 18-20°C for histological examination. Staining them showed no autolytic damage, with no difference between stretched and unstretched strips form the same body (MacKay, Banks, Sykes & Lee, 1978).

Force was expressed as a force/unit area of stress (N/m²). At ‘zero load length’ the mean cross-sectional area of the vessel strip was calculated as the width multiplied by average thickness, obtained by dividing the weight of the strip by its dimensions (25 mm × 10 mm), assuming a tissue density of 1.06 (McDonald, 1974).

Stretching the vessel strip in the tension balance caused its free edges to become concave as the strip lengthened. The mean cross-sectional area of each measured stretched length of the strip was calculated by assuming that the original volume of tissue between the clamps remained unchanged. The error this assumption made to the stress calculations was examined in six pairs of vessel strips. A rectangle of dots was marked with Indian
ink upon the surface of the mid-portion of the vessel strip when mounted in the tension balance. The strip was then photographed at each load for subsequent measurement.

**Results**

The percentage increase in vessel circumferential length was plotted against the applied stress (N/m²) with interpolations at specified stress, allowing comparison between subjects. These values were then grouped by age, in decades (Tables 1 and 2). The mean values of extension at increasing stress showed that the pulmonary arteries and pulmonary veins behaved differently (Fig. 2).

At all ages pulmonary arteries were more extensible than pulmonary veins; thus the arterial circumferential length in the age group 40–49 years increased by 37.7 ± 2.8% at a stress of 10 × 10⁴ N/m², whereas pulmonary veins stretched only by 8.5 ± 0.9% in the same age group at this load.

Both pulmonary arteries and pulmonary veins

### Table 1. Percentage extension of circumferential strips of pulmonary artery

Mean values (with se) are given at specific loads at different ages.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>10⁻⁴ × Extending force (N/m²)</th>
<th>Extension (%)</th>
<th>No. of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Under 20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13-9</td>
<td>(1.34)</td>
<td>23.2</td>
<td>30.1</td>
</tr>
<tr>
<td>20–29</td>
<td>(1.56)</td>
<td>22.1</td>
<td>28.6</td>
</tr>
<tr>
<td>30–39</td>
<td>(1.91)</td>
<td>16.5</td>
<td>21.3</td>
</tr>
<tr>
<td>40–49</td>
<td>(1.19)</td>
<td>17-4</td>
<td>22-1</td>
</tr>
<tr>
<td>50–59</td>
<td>(1.12)</td>
<td>17-6</td>
<td>22-3</td>
</tr>
<tr>
<td>60–69</td>
<td>(1.55)</td>
<td>21-1</td>
<td>25-6</td>
</tr>
<tr>
<td>70–79</td>
<td>(0.98)</td>
<td>15-3</td>
<td>18-5</td>
</tr>
<tr>
<td>Over 80</td>
<td>(0.81)</td>
<td>12-4</td>
<td>14-6</td>
</tr>
</tbody>
</table>

### Table 2. Percentage extension of circumferential strips of pulmonary vein

Mean values (with se) are given at specific loads at different ages.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>10⁻⁴ × Extending force (N/m²)</th>
<th>Extension (%)</th>
<th>No. of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Under 20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6-9</td>
<td>(1.44)</td>
<td>8-9</td>
<td>10-2</td>
</tr>
<tr>
<td>20–29</td>
<td>(1.07)</td>
<td>6-4</td>
<td>7-2</td>
</tr>
<tr>
<td>30–39</td>
<td>(1.65)</td>
<td>5-4</td>
<td>6-7</td>
</tr>
<tr>
<td>40–49</td>
<td>(0.58)</td>
<td>3-2</td>
<td>4-5</td>
</tr>
<tr>
<td>50–59</td>
<td>(0.84)</td>
<td>2-7</td>
<td>3-4</td>
</tr>
<tr>
<td>60–69</td>
<td>(0.75)</td>
<td>3-1</td>
<td>4-1</td>
</tr>
<tr>
<td>70–79</td>
<td>(0.67)</td>
<td>4-4</td>
<td>5-8</td>
</tr>
<tr>
<td>Over 80</td>
<td>(0.54)</td>
<td>2-9</td>
<td>3-9</td>
</tr>
</tbody>
</table>
Fig. 2. Stress–strain measurements of circumferential strips of main pulmonary artery (—) and pulmonary vein (——) from patients after death from conditions other than heart or lung disease. Mean values are shown for each age group (years): <20 (○); 20–29 (●); 30–39 (□); 40–49 (■); 50–59 (○); 60–69 (●); 70–79 (△); >80 (▲). SEM values are also shown for the arterial studies at a force of 20 × 10⁴ N/m².

became less extensible with age, particularly as the loads increased (Fig. 3 and Fig. 4). The striking difference in extensibility between the pulmonary arteries and pulmonary veins was preserved at all ages. The veins were largely inextensible at all ages. The arteries tended to lose their extensibility with age.

Calculations and discussion

The basic premise of our study was that the pulmonary veins could protect lung capillary blood flow pulsatility from attenuation by retrograde conduction of left atrial pressure events during the cardiac cycle. This was suggested by observations in rabbit lungs by Caro & Saffman (1965), who showed that large pulmonary veins had an extremely non-linear pressure/volume relationship. When the pressure within the large pulmonary veins was raised from 0 to 5 cm water there was an initial increase in diameter, suggesting that the large veins could change their volume considerably when submitted to physiological pressure changes. The veins soon reached the limit of their distensibility. However, the authors did not measure vein diameters at very low distending pressures, their pressure/volume curves below 5 cm water being an extrapolation. However, at pressures above 5 cm water they found that rabbit pulmonary veins behaved much as we have found in human veins, with very little distensibility under increasing internal pressures.

Although we have studied only post-mortem material, histological examination showed good preservation with no autolytic change in the vessels. Furthermore we found no significant relationship between the incremental modulus calculated from the ratio of stress to strain (see eqn. 2 below) and the time since death and removal of the tissue. Clearly we cannot presume that living tissue behaves similarly because the active contribution of living smooth muscle within the media was absent in our studies. It was impossible to obtain sufficiently large pieces of vessel from surgical specimens to enable similar measurements to be made on living human tissue.

To examine the physiological relevance of these measurements it is necessary to translate stress–strain relationships to relationships between intravascular pressure and volume. In the tension-balance experiments vessel strips were subjected to an extending load, which thus created a tension in the vessel strip. This tension \( T \) is distributed throughout the cross-sectional area \( A \), the resultant wall stress \( S \) therefore being \( T/A \). The strip forms a section of the circumference of the whole vessel in life. If the ratio of the wall thickness to the radius of the vessel under physiological pressures is less than 0.15 the circumferential stress \( S \) within the wall of an isotropic vessel may be approximated by the Laplace equation (McDonald, 1974):

\[
S = \frac{P \cdot R}{h} \tag{1}
\]

where \( P \) = distending pressure (N/m²), \( R \) = mean radius of vessel (m) and \( h \) = wall thickness (m).

Vessel wall thickness was estimated from the volume, weight and density of the strips measured at the time of tension-balance studies, as recommended by McDonald (1974). Since the length of each strip was measured directly in the tension balance at each load increment by using a travelling microscope, and since the volume and density of the tissue remained constant (Carew,
Fig. 3. (a) Changes taking place with age in the percentage extension of pulmonary artery strips submitted to a force of $5 \times 10^4$ N/m$^2$ (extension = regression coefficient $\times$ age + intercept). Regression coefficient = $-0.284$. Intercept = 43.47. Correlation coefficient = $-0.677$. Confidence limits = ±0.0343. (b) Changes taking place with age in the percentage extension of pulmonary vein strips subjected to a force of $5 \times 10^4$ N/m$^2$ (extension = regression coefficient $\times$ age + intercept). Regression coefficient = $-0.074$. Intercept = 11.33. Correlation coefficient = $-0.339$. Confidence limits = ±0.0267.

Vaishnav and Patel, 1968; McDonald, 1974), the wall thickness at different loads could also be calculated.

A mean wall thickness calculated from the weight of the strip was used to calculate stress, as we could not measure wall thickness. Moreover, Apter, Rabinowitz & Cummings (1966) found considerable variation in wall thickness of vessel rings measured histologically, for with weighing techniques (McDonald, 1974) the adventitia has to be removed and it is rarely possible to remove it cleanly.

The unstressed thickness of the pulmonary arteries was 0.4 ± 0.08 mm and of pulmonary veins 0.27 ± 0.14 mm. The original mean radius of the vessels in situ must also be estimated to calculate ‘intravascular pressure’. Unfortunately estimation of the initial radius of either the intact pulmonary artery or vein is subject to considerable error, as the longitudinal forces affect both the unstressed length and the radius. There are also circumferential stresses at zero transmural pressure, which also cannot be estimated accurately (McDonald, 1974). Thus we can give only a range of values for the likely radii in vivo of the vessels that we have studied post mortem. The minimum radii of the vessels were estimated by splitting them open longitudinally and measuring their circumference (Wesley, Vaishnav, Fuchs, Patel & Greenfield, 1975). The radius of the pulmonary arteries was 6.96 ± 1.01 mm and that of the pulmonary veins 4.94 ± 0.95 mm. These estimated values of vessel radius, wall thickness and wall stress then yielded probable equivalent intravascular pressures and wall stresses for vessels by eqn. (1). Thus in a pulmonary artery of radius 7 mm and a wall thickness to radius ratio of 0.1, a mean intravascular pressure of 20 mmHg corresponds to a wall stress of $1.8 \times 10^4$ N/m$^2$, equivalent to a load on the circumferential strip of 13 g.
Attenuation of pressure and flow waves travelling down a vessel will depend partly upon Young's modulus of elasticity \((E)\) defined as:

\[
E = \frac{F/A}{(\Delta l/l_0)} \tag{2}
\]

where \(F\) = force (N), \(A\) = cross-sectional area of the tissue (m²), \(\Delta l\) = change in tissue length (m), \(l_0\) = the unstretched length of tissue (m), \(E\) = Young's modulus (N/m²).

If the relationship between stress \((F/A)\) and strain \((l/l_0)\) is linear, then the slope of the line relating them is Young's modulus. Eqn. (2) can be applied to a vessel with a circular cross section by equating \(L_0\) to \(2\pi r_0\), where \(r_0\) is the unstressed initial radius at zero transmural pressure, and \(F\) is the wall tension calculated from the transmural pressure and radius (eqn. 1).

Estimation of the initial radius is subject to considerable errors, as discussed earlier, and the curve relating stress to strain was curvilinear so that there was no single value of Young's modulus. However, the slope of the tangents to the stress–strain curve at physiological values of stress can be calculated and these are known as the incremental modulus (Bergel, 1961). Direct measurements of the volume distensibility of segments of blood vessels (Patel,
Greenfield & Fry, 1964; Wesley et al., 1975) can partly overcome these problems but the main pulmonary veins that we studied were too short for this.

The error introduced in the calculation of stress by the tendency of the free edges of the vessel strips to become concave as the strips were extended in the tension balance were estimated from photographs made on six strips. The vein strips were so inextensible that no significant difference was found between stresses calculated from measurement made upon the whole strip, which assumed constant width, and measurements made from changes in the dimensions of the central rectangle marked on the strip. In the case of the pulmonary artery the stress calculated from measurements made from the whole vessel strip, assuming a constant width, were up to 30% lower compared with stresses calculated from the central rectangle, which took into account changes in width. The changes in width responsible for these errors were almost complete before loads of physiological interest were reached. Thereafter the changes in vessel width were small and since the incremental modulus was calculated from the difference of two consecutive stresses the calculated values of the modulus was much less affected. Thus at a load of 15 g the calculated incremental modulus for the whole strip was $1.8 \times 10^4$ N/m², whereas that of the central rectangle was $2.2 \times 10^2$ N/m². We found that the incremental modulus of the pulmonary artery in the 20–30 years age group at a stress of $3 \times 10^4$ N/m² was $1.78 \times 10^4$ N/m². This increased to $5.1 \times 10^4$ N/m² in the over-80 years age group. The elastic modulus can also be used to estimate the velocity of pressure and flow waves in vessels, from the Moens–Korteweg equation (McDonald, 1974) where:

$$C_0 = \frac{Eh}{2R\rho}$$

where $C_0 = \text{wave velocity (m/s)}$, $E = \text{modulus of elasticity (N/m²)}$, $h = \text{wall thickness (m)}$, $R = \text{radius (m)}$, $\rho = \text{density (kg/m³)}$.

We calculated the wave velocity in the pulmonary artery to be 2.24 m/s in those aged 20–30 years and 3.81 m/s for those over 80 years. The value for the incremental modulus is similar to that measured at operation for human pulmonary artery by Patel et al. (1964), who found a value of $163 \text{ g/cm²}$ for the static elastic modulus of a pulmonary artery with a ratio of wall thickness to radius of 0.10. This is equivalent to an incremental modulus of $1.6 \times 10^5$ N/m² (McDonald, 1974).

Similar calculations can be made for a pulmonary vein 5 mm in radius with a ratio of wall thickness to radius of 0.1. The smallest load that could be applied to the vein strips was 2.5 g, corresponding to a wall stress of $1–1.5 \times 10^4$ N/m² and an intravascular pressure of 9–12 mmHg (eqn. 1). These values can only be approximate as the wall thickness of the pulmonary veins could not be measured precisely by dissecting off superficial connective tissue without stripping part of the vein wall itself. The incremental modulus and wave velocity at a stress of $1 \times 10^4$ N/m² were $2.2 \times 10^2$ N/m² and 3.22 m/s respectively and at a stress of $2 \times 10^4$ N/m² were $5.3 \times 10^4$ N/m² and 5.0 m/s. The incremental modulus was similar to that calculated by Wesley et al. (1975) in jugular veins of dogs. The incremental modulus of the pulmonary veins showed no significant change with age. We found the relative changes in incremental modulus and wave velocity of the pulmonary arteries with age were similar to those in human systemic arteries (Learoyd & Taylor, 1966). The wide variations from case to case found by Learoyd & Taylor (1966) were presumed to arise from the difficulty of measuring wall thickness. They found that the static modulus of elasticity of the thoracic aorta from old subjects was about four times that of a younger age group. McDonald (1974) found that the minimum transmission per wavelength in an artery 10 mm in diameter was 20%. If we assume a wave velocity as low as 2 m/s the wavelength at 1 Hz is 2 m. The proportion of a left atrial pressure wave that should be transmitted over a distance of approximately 15 cm from the left atrium to the lung capillaries is $E^{-1.6 \times 15/200}$ or 89%. Such a high transmission ratio is unlikely on the basis of the earlier clinical observation of Gillespie et al. (1967). Moreover, attenuation of pressure and flow waves in normal pulmonary veins cannot be predicted from these elastic moduli because the normal mean left atrial pressure is between 4 and 12 mmHg, so that the veins may not be in a fully distended state (Braunwald, Brockenborough, Frahm & Rose, 1961; Samet, Bernstein, Medow & Levine, 1965).

The above discussions show that although wave attenuation in arteries and veins is likely to be similar when the vessels are fully distended at high pressures, the attenuation of pressure and flow waves transmitted from the lung capillaries to the pulmonary veins and left atrium cannot be predicted from our data on isolated veins when normal left atrial pressures are considered. These pressures are normally lower than the lowest equivalent pul-
monary venous distending pressure that we estimate to exist at the stress applied at 'zero load length'. Moreover, the stress–strain measurements of veins at all ages showed them to be virtually inextensible.

Thus some other hypothesis than vascular distensibility must be proposed to explain how phasic left atrial pressure changes normally fail to be transmitted retrogradely, so that the time course of lung capillary blood flow throughout the cardiac cycle remains independent of left atrial pressure events (Gillespie et al., 1967; Karatzas & Lee, 1970).

Let us suppose that the large pulmonary veins close to the left atrium behave as collapsible rather than distensible structures. If their combined capacity were large enough, then they could together act as a reservoir which changed volume over a very narrow pressure range, determined only by the transmural pressure necessary to deform the walls of the veins. In this way episodic rises in left atrial pressure, which might otherwise impede inflow into the atrium, would be accompanied by uninterrupted filling of the extraparenchymal pulmonary veins from the lung capillaries. During periods of low left atrial pressure the large extraparenchymal pulmonary veins would be isolated from the left atrium. Thus the presence of readily collapsible pulmonary veins close to the left atrium would effectively isolate left atrial pressure changes from affecting flow characteristics in the pulmonary capillaries. This hypothesis has been verified by measurements of the cross-sectional dimensions of pulmonary veins in open-chested dogs by an ultrasonic technique (Bertram, Lee, Rajagopalan & Stallard, 1977). The cross-sectional shape of the large pulmonary veins external to the lung parenchyma was found to change from a circle or wide ellipse to a narrower ellipse, or to collapse altogether during rapid atrial filling.

Acknowledgments
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References


