In Vivo Pressure-Radius Relationships of the Pulmonary Artery in Children with Congenital Heart Disease

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SUMMARY

The effects of either increased pulmonary artery blood flow or pressure on the magnitude of the radius and the dynamic properties of the right pulmonary artery were studied angiographically in 162 patients during cardiac catheterization. Patients were divided into seven groups according to their hemodynamic findings. The right pulmonary artery radius was measured during systole and diastole, from the projected films, at the midpoint between the bifurcation of the main pulmonary artery and the bifurcation of the right pulmonary artery. The mean pulmonary artery radius was increased in patients with either increased pulmonary blood flow or pressure, and in patients with isolated valvular pulmonic stenosis. Both the pressure-strain elastic modulus (stiffness index) and the tension-radius regression were different from normal only in patients with increased pulmonary artery pressure regardless of the pulmonary blood flow. This finding indicates that the pulmonary artery is stiffer in patients with pulmonary hypertension but that its elastic properties are not altered secondarily to increased blood flow.

Additional Indexing Words:
Pulmonary artery distensibility

Congenital heart defects often are associated with either increased pulmonary artery blood flow, blood pressure, or both. Heath et al.1 2 and Edwards3 have described abnormal histologic changes in the pulmonary arteries in various congenital heart diseases. However, there are no quantitative data obtained in vivo relating the effects of altered blood flow and pressure on the dynamic properties of the pulmonary artery. This information must be known in order to formulate a realistic model of the pulmonary circulation in man. In addition, changes in pulmonary artery mechanics in various congenital heart diseases may be of interest in defining the pathogenesis of pulmonary obstructive disease. The purpose of this investigation was to evaluate the magnitude of the mean radius and the pressure-radius relationships of the right pulmonary artery both in children with normal pulmonary flow and pressure and in those having various congenital heart diseases with altered pulmonary hemodynamics.

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General and Hemodynamic Data

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of patients</th>
<th>Age (years)*</th>
<th>Body surface area (m²)*</th>
<th>Heart rate (beats/min)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Normal right heart</td>
<td>60</td>
<td>6.3</td>
<td>0.83</td>
<td>112</td>
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<tr>
<td></td>
<td></td>
<td>(0.2–16.0)</td>
<td>(0.22–1.99)</td>
<td>(65–167)</td>
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<td>2. Atrial septal defect</td>
<td>14</td>
<td>6.7</td>
<td>0.86</td>
<td>104</td>
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<tr>
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<td></td>
<td>(3.0–14.0)</td>
<td>(0.55–1.40)</td>
<td>(83–136)</td>
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<td>3. Ventricular septal defect (low pressure)</td>
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<td>6.6</td>
<td>0.83</td>
<td>113</td>
</tr>
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<td></td>
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<td>(0.23–1.46)</td>
<td>(67–167)</td>
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<tr>
<td>4. Ventricular septal defect (high pressure)</td>
<td>30</td>
<td>3.0</td>
<td>0.50</td>
<td>124</td>
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<tr>
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<td></td>
<td>(0.1–13.0)</td>
<td>(0.21–1.15)</td>
<td>(68–167)</td>
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<tr>
<td>5. Patent ductus arteriosus</td>
<td>6</td>
<td>1.5</td>
<td>0.38</td>
<td>134</td>
</tr>
<tr>
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<td></td>
<td>(0.2–6.0)</td>
<td>(0.23–0.72)</td>
<td>(107–150)</td>
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<tr>
<td>6. Pulmonary hypertension</td>
<td>7</td>
<td>5.1</td>
<td>0.67</td>
<td>124</td>
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<tr>
<td></td>
<td></td>
<td>(0.4–14.0)</td>
<td>(0.41–1.49)</td>
<td>(107–150)</td>
</tr>
<tr>
<td>7. Pulmonary stenosis</td>
<td>19</td>
<td>6.5</td>
<td>0.82</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.4–14.0)</td>
<td>(0.33–1.41)</td>
<td>(70–150)</td>
</tr>
</tbody>
</table>

Abbreviations: QP/QS = pulmonary to systemic blood flow ratio; $E_p$ = pressure-strain elastic modulus.

*Mean values and ranges.

†Mean values ± 1 SEM.

‡Values significantly different ($P < 0.01$) from normal.

**Figure 1**

In the lower panel, measurements of the right PA radius from each frame of the cineangiogram are indicated by dots. Note the similarity between the line connecting these dots and the simultaneously recorded PA pressure. Abbreviations: EKG = electrocardiogram; Rt. = right.

**Methods**

The data were obtained during routine diagnostic cardiac catheterization in 162 patients. Informed consent as to the nature of the procedure was obtained.
investigation was obtained from the patients' parents. Patients were divided into seven groups according to hemodynamic data (Table 1). Group 1, 60 patients, consisted of 36 children with normal hearts who had either a vascular ring, sequestration of the lung, or an abnormal electrocardiogram without other demonstrable cardiac abnormalities. The group also contained 14 patients with isolated valvular aortic stenosis, and 10 patients with coarctation of the aorta. Patients in group 1 served as the control group. All of these children had both a normal pulmonary artery (PA) pressure and pulmonary vascular resistance index (mm Hg/liter/min/m²) and mean PA pressure (mm Hg). The systolic PA pressure in this group was less than 30 mm Hg, and all but four patients had PA pressures less than 20 mm Hg. Group 2 consisted of 14 patients with an isolated atrial septal defect (ASD), an increased pulmonary systemic flow ratio (QP/QS > 1.5), and a normal mean PA pressure. Group 3 contained 26 patients with an isolated ventricular septal defect (VSD), an increased QP/QS ratio and a normal mean PA pressure. Group 4 had 30 patients with an isolated ventricular septal defect, an increased QP/QS ratio, and an elevated pulmonary artery pressure (mean PA pressure > 25 mm Hg). Group 5 contained six patients with a patent ductus arteriosus (PDA) with both increased QP/QS ratio and mean PA pressure. Group 6 had seven patients with pulmonary hypertension (PH). Mean PA pressure in this group ranged from 45 to 70 mm Hg. Four of these patients had no shunt, and three had an intraventricular shunt with QP/QS ratio < 1.5. Group 7 contained 19 patients with isolated valvular pulmonic stenosis (pulmonary valvular gradient > 30 mm Hg), and a normal mean PA pressure. The cardiac output was not obtained in this group.

All patients were studied in the supine position. Patients less than six months of age were premedicated with meperidine (1 mg/kg) and either promethazine (0.5 mg/kg) or Chlorpromazine (0.5 mg/kg), and were not given general anesthesia. The remaining subjects were premedicated with secobarbital (1.5 mg/kg), and received light general anesthesia with nitrous oxide, oxygen and halothane (< 0.5%). Expired air was collected in the usual manner for the measurement of oxygen consumption. Oxygen content of blood samples obtained from the superior and inferior vena cava, pulmonary artery, and aorta were used to determine the pulmonary (QP) and systemic flow (QS) by the Fick method, with standard formulae. These samples were drawn before the cineangiogram (cine) was obtained. An electrocardiogram (ECG) was recorded in all patients during the study. The right PA pressure and left ventricular (LV) pressure were measured using NIH catheters (sizes 5–7) and Statham P23-AA transducers immediately prior to injection of contrast media.

After injection of 1.25 ml/kg of 75% Hypaque-M* into the patient's pulmonary artery, we obtained cineangiograms, using an anteroposterior (AP) projection and 16 mm film at 60 frames per sec. A photocell device sensitive to the X-ray pulse was utilized during the filming sequence to synchronize the cine frames with the other

* Sodium and meglumine diatrizoates, Winthrop Laboratories, New York, N. Y.
recorded data. Left ventricular pressure, PA pressure, photocell output, and ECG were recorded on both a Sanborn oscillograph and a Sanborn (2000 series) electromagnetic tape recorder. After each study a metal grid with 625 squares (1 cm x 1 cm) was filmed parallel to the AP tube at the position occupied by the heart. The grid image was used to correct for linear X-ray magnification and to evaluate the nonlinear distortion. Since there was no measurable distortion of the grid in the inner three-fourths of the projected image, measurements were limited to this area. The details of this system have been described previously.5

The effect of contrast media injection on the PA pressure was examined in two patients with normal pressure and two patients with pulmonary hypertension. Two catheters were positioned in the pulmonary artery so that pressures could be recorded during the injection of contrast media. Because there was no detectable change in the PA pressure during injection in any of these patients, it was felt that the PA pressure recorded immediately prior to the injection was representative of the pressure existing during filming. To lend further validity to the pressure-radius relation, in these four patients the radius was obtained for each frame for 3 consecutive beats immediately after contrast media injection. Figure 1 shows a simultaneous recording of the right PA radius and pressure for 1 beat in a six-year-old child with high pressure VSD, and demonstrates the marked similarity in contour of these two parameters. Thus, in the remainder of the patients, a single catheter was used for recording PA pressure and for injection of contrast media. Patients having more than a 5 beats/min difference in heart rate between the pressure recording and the cine were excluded from the study.

In evaluating the cineangiographic data, the right pulmonary artery was chosen because of its relatively cylindrical shape and easily identifiable fixed points during both systole and diastole. The right PA radius was measured at the midpoint between the bifurcation of the main PA and the bifurcation of the right PA. The right PA radius was measured at both maximal and minimal sizes for the first 3 consecutive beats after contrast media injection. There was no significant beat-to-beat variation, and the average values of maximum and minimum radius were used for analysis. The mean right PA radius (R) was computed as the average of minimum and maximum radius values. The change in radius (∆R) was the difference between the maximum and minimum radius values. The actual size of the PA was calculated using the correction factor from the grid, as noted above. Mean PA pressure (P) was obtained at the time of recording by electrically integrating the pulsatile pressure. PA pulse pressure (∆P) was measured as the difference between the systolic and diastolic pressure.

The following were computed:

1. Per cent change in radius (PCR) (%):

\[
PCR = \frac{∆R \times 100}{R}
\]

2. Pressure-strain elastic modulus (Ep) (g/cm²):

\[
Ep = \frac{∆P \times R}{∆R}
\]

3. Mean tension (T) (g/cm):

\[
T = \frac{P \times R}{C}
\]

4. Pulmonary vascular resistance index (PVR) (mm Hg/liter/min/m²):

\[
PVR = \frac{P - \text{left ventricular end-diastolic pressure}}{Q/PBSA}
\]

where BSA equals body surface area. The body surface area in m² was obtained as described by Dubois.7 The mean values of ∆P, PCR, and Ep for each group were compared to the normal patient group using a one-way analysis of variance. Additional relationships were examined using a quadratic polynomial regression scheme.8

Results

Pertinent data describing the patient groups are listed in table 1.

The size of the right PA radius might be affected by either PA pressure or flow, and it should vary with the patient's BSA. In order to account for the size differences, a regression of the mean PA radius (y) and BSA (x) was examined separately for each group. The regression of the radius was significantly different in the normal group (P < 0.001) from all the other groups. Figure 2 illustrates the radius versus body surface area regression for each group and demonstrates that for a given BSA the radius is smallest in the normal group. A comparison of low and high pressure VSD patients (groups 3 and 4) revealed that the radius is larger in the high pressure VSD group (P < 0.001). The radius versus BSA regression in the low pressure VSD group was significantly different (P < 0.001) from the ASD patients.

It is apparent that some of the variables, particularly those involving PA radius, could

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A regression line and one standard deviation relating the mean right PA radius as a function of body surface area is given for each patient group. In both the normal group and low pressure VSD groups the regression line was curvilinear indicating that the PA radius does not increase after the patient BSA reaches 1.2 m². In the other groups this was not demonstrated due to the lack of a significant number of larger patients (BSA > 1.2 m²). Abbreviations: Normal = normal right heart; LP VSD = low pressure ventricular septal defect; HP VSD = high pressure ventricular septal defect; PH = pulmonary hypertension; PDA = patent ductus arteriosus; PS = calcular pulmonary stenosis; ASD = atrial septal defect.

Discussion

De La Cruz et al.⁹ have studied the size of the main pulmonary artery in man using

be affected by the age or size of the patient. Since patient size varies from group to group and within groups, it was necessary to take this variation into account. The possible dependence of $E_p$ on BSA was examined in normal patients since this was the largest group, and contained a wide range of BSA values. A quadratic regression analysis of $E_p$ (y) and BSA (x) was performed. Neither the slope nor the quadratic term was significantly different from zero, and as a result, it was concluded that $E_p$ was not dependent on BSA. A similar analysis was performed using the PCR, and no dependence on BSA was demonstrated. On this basis, it seems reasonable to assume that group differences in $E_p$ or PCR were not related to differences in BSA.

The per cent change in radius (table 1) was not significantly different from normal in any group except in the group with pulmonary stenosis where it was less ($P < 0.001$) than normal. The $E_p$ was greater than normal in patients with increased pulmonary artery pressure and increased pulmonary vascular resistance (table 1, groups 4, 5, and 6). $E_p$ did not differ significantly from normal in the remaining groups.

The tension-radius regression analysis indicated that there were significant group differences. However, the group differences seemed to be related to mean PA pressure regardless of the pulmonary flow. Thus, all patients were divided into the following three groups according to mean PA pressure: normal (<25 mm Hg), moderate elevation (26–50 mm Hg), and severe elevation (>50 mm Hg). The results of this analysis are illustrated in figure 3. These data indicate that the mean tension in the pulmonary artery is uniformly increased in patients with elevated PA pressures regardless of the pulmonary blood flow.
autopsy material, and found its diameter to be about the same as the right PA in our patients. However, their measurements were made without a pressure stress and, in addition, the changes secondary to fixing of the tissues must be considered. Thus, the data of De La Cruz et al. cannot be compared to our series. The present study provides the first in vivo quantitative data on the radius of the right pulmonary artery in normal children and in those with congenital heart diseases. The fact that the mean PA radius was increased in patients with either an elevated pulmonary flow (groups 2, 3) or pressure (group 6) indicates the independent effect of increased flow or pressure on the size of the pulmonary artery.

Furthermore, the increased radius found in high pressure VSD patients (group 4) as compared with low pressure VSD patients (group 3) indicates the effect of both flow and pressure. Thus, either an increase in flow or pressure or both will result in an increase in the radius of the pulmonary artery.

Of additional interest is the larger radius found in ASD patients as compared with low pressure VSD patients. This finding could not be explained by a difference in the QP/QS ratio or PA pressure because these two variables were not significantly different in the two groups. One can speculate that the difference in radius in the two groups is related to a difference in instantaneous flow profile in the pulmonary artery.

The increased radius in the right pulmonary artery seen in patients with pulmonary steno-
sis may be due to turbulence producing a high
density lateral stress on the vessel wall. The
decreased flow rate and prolonged ejection
across the stenotic pulmonic valve will result
in a small PA pulse pressure and change in
radius (table 1).

The normal percentage change in radius
found in patients with elevated pulse pres-
        |   sure (groups 4, 5, 6) suggests a decreased
distensibility of the pulmonary artery in these
patients. The percentage change in radius
reported here is similar to values obtained by
Patel et al.,10 who used a caliper to directly
measure the vessel radius of the dog PA. Data
were also recorded by Greenfield et al.,11 who,
using the same method in the PA of human
patients with a mean age of 41 years, found a
change in radius slightly less than found in the
present study.

The elastic behavior of a substance is
usually defined by Young's modulus (E): 6

\[ E = \frac{E_p}{h} \]

where h is the wall thickness. Since the wall
thickness could not be obtained in this study,
a pressure-strain elastic modulus suggested by
Peterson et al.6 was calculated. The value of
E_p in the normal group was similar to that
found in the dog PA by Patel et al.10
Greenfield et al.,11 using the recording caliper,
obtained an average E_p of 160 g/cm^2 in the
main pulmonary artery of human patients.

These results are not significantly different
from ours, and their similarity adds validity to
the measurements reported in the present
study. The fact that the value of E_p was
larger than normal in all patients with
increased PA pressure regardless of the
pulmonary flow indicates that the increased
stiffness of these vessels was pressure-depen-
dent. This is emphasized further by the
tension-radius relationships (fig. 3), which
was only abnormal in patients with elevated
PA pressures. These data indicate that the
pulmonary artery wall is stiffer and less
distensible in patients with pulmonary hyper-
tension than it is in patients with normal PA
pressures.

It is possible that the contrast media might
affect the properties of the vascular wall and
lead to error in data. In four patients, no
change occurred in the PA pressure in the 10
beats following the injection. The PA radius
was obtained in the first 3 beats, and no
change was noted in either the radius or
stiffness index in these beats, indicating that
the contrast media did not alter the pulmo-
nary artery dynamics during the period of
measurement.

Many factors could be responsible for an
increase in stiffness of the vessel wall. An
increase in heart rate10,12 would decrease the
apparent distensibility of the wall. However,
the data of Patel10 and Bergel12 indicate that
in the physiological range of heart rates found
in the present study there would be no rate
effect on the elasticity of the vessel. Further-
more, the heart rates were similar in the
different groups (table 1).

Peterson et al.6 indicated that physiological
variations in the mechanical properties of
arteries could be accomplished by neurohu-
moral influences upon smooth muscles. It is
very unlikely that this factor accounts for the
differences in our patients since they were
studied under similar conditions.

Heath et al.2 showed that the PA wall
thickness in patients with pulmonary hyper-
tension was nearly double the wall thick-
ness in patients with normal PA pressure
(pulmonary stenosis and tetralogy of Fallot).
If a similar relation for the wall thickness
existed in our patients, then the value of
Young's modulus in groups 4 and 6 would be
about 1.5 and 2 times the normal group,
respectively, indicating that a doubling of wall
thickness alone would not explain the in-
creased stiffness in the PA noted in patients
with pulmonary hypertension.

It has been shown that the vessel wall
becomes progressively stiffer (higher elastic
modulus) the more it is stretched.13-17 Thus,
the stiffness of the wall in a given vessel
depends on its location in the pressure-radius
(strain-stress) curve. Although the pressure
could not be raised or reduced in these groups
of patients to facilitate group comparison at
similar pressure ranges, the data indicate that for an equal radius the wall is stiffer in patients with pulmonary hypertension than it is in patients with normal PA pressure. The alteration in pulmonary artery hemodynamics resulted in a decreased distensibility and an increased PA pulse pressure (table 1), and thus acted as a stimulus to medial hypertrophy as well as irreversible intimal changes in the pulmonary arterioles seen in patients with longstanding pulmonary hypertension.

These data indicate the need for further investigation regarding the relationship between the physical characteristics and histological structure of the PA wall. Of particular interest in this regard will be the time course of changes in PA stiffness indices and wall histology after correction of cardiac defects associated with elevated PA pressure. Answering these questions may lead to a better understanding of the pathogenesis of pulmonary vascular disease.

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References


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