Effects of Oxygen Breathing on Pulmonary Vascular Input Impedance in Patients with Pulmonary Hypertension*

Takashi Haneda, M.D.; Toshiyuki Nakajima, M.D.; Kunio Shirato, M.D.; Sachio Onodera, M.D.; and Tamotsu Takishima, M.D., F.C.C.P.

The effect of oxygen breathing on the stiffness of the large pulmonary artery has not been elucidated. We analyzed the proximal pulmonary arterial impedance with a multisensor catheter in ten patients with pulmonary arterial hypertension (PAH), eight patients with pulmonary venous hypertension, and six control subjects. The stiffness of the vessel was quantified by the characteristic impedance (Zo) and compared with the plasma norepinephrine level. Ten minutes of high-oxygen breathing decreased the Zo (from 78 ± 18 to 57 ± 14 dynes•sec•cm⁻⁵, p<0.01) and pulmonary arterial resistance in all the cases with PAH. In this group, norepinephrine also decreased (from 381 ± 59 to 319 ± 77 pg/ml, p<0.01) following the correction of hypoxemia. Yet, those parameters did not change in the other two groups. These results indicate that in patients with PAH, oxygen breathing can reduce the stiffness of the main pulmonary artery because of the sympatholytic effect.

Although the dilating effect of oxygen on pulmonary vascular beds has been documented in patients with pulmonary arterial hypertension, it is still unclear whether oxygen affects the large pulmonary arteries in those patients. One might assume that the large pulmonary arteries would not respond to hypoxemia, since even highly concentrated oxygen in alveoli would not directly reach those vessels. Others might postulate that oxygen increases the vascular tone of the large pulmonary arteries, since the systemic vascular resistance has been observed to increase during high oxygen breathing. Third, it is also possible that the stiffness of those vessels would be reduced by oxygen in pulmonary hypertensive patients who show hypoxemia, because the correction of hypoxemia can attenuate the sympathetic excitability in patients with chronic cor pulmonale.

Alterations in mechanical properties of the proximal pulmonary vessels will change the pressure-flow relationship in phase and magnitude and may alter the opposition to pulsatile flow. It is well-known that pulmonary vascular input impedance is the major portion of right ventricular afterload, and any intervention to patients with pulmonary hypertension should take into consideration the change in the impedance spectra. Therefore it is important to know how the large pulmonary arteries respond to oxygen breathing. To clarify this question, we analyzed the pulmonary arterial input impedance in patients with pulmonary hypertension using a multisensor catheter, and examined the stiffness of the vessel by the characteristic impedance before and during oxygen breathing. We also measured the plasma norepinephrine levels in them and discussed the relation of the stiffness to the sympathetic nerve tone.

Materials and Methods

Selection of Patients and Cardiac Catheterization Procedures

Eighteen patients with pulmonary hypertension (mean pulmonary arterial pressure ≥25 mm Hg) and six with normal pulmonary circulation were involved in this study. They were classified into the following three groups: (1) six patients with normal pulmonary arterial mean pressure (PAP) and normal pulmonary capillary wedge pressure (PCWP) served as controls (control group); (2) the second group had pulmonary venous hypertension, with elevated PCWP ranging from 14 to 31 mm Hg and elevated PAP within a range of 25 to 41 mm Hg (PVH group) and (3) the third group had pulmonary arterial hypertension, with normal PCWP ranging from 2 to 13 mm Hg and elevated PAP within a range of 25 to 60 mm Hg (PAH group). General patient characteristics and basic blood gas levels appear in Table 1. There were no significant differences in age, body surface area, or in Paco₂ or pH in arterial blood in all three groups. However, Paco₂ in arterial blood was significantly lower in the PAH group than in the control and PVH groups. None of the patients had been given any sympathomimetic or sympatholytic medication. Informed consent was obtained from each subject after the nature and the purpose of the protocol had been explained.

Diagnostic cardiac catheterization was performed with subjects in the fasting state without any premedication. A multisensor catheter (Millar, VPC-664 A) was inserted into the pulmonary trunk through the left antecubital vein. This catheter was mounted with an electromagnetic flow velocity sensor and a pressure transducer 5 cm distal from its tip. The tip was then advanced further into either the left main or the right main pulmonary artery, and the sensors were positioned fluoroscopically near the upper border of the sinuses of the pulmonary trunk. This arrangement minimized the movement of the sensors in the blood vessels. The catheter's position was considered satisfactory if there were no sudden movements during the cardiac cycle noted during fluoroscopy and if there was a steady flow.
### Table 1—Patient Characteristics and Blood Gas Levels*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age, yr</th>
<th>Sex</th>
<th>BSA, m²</th>
<th>Diagnosis</th>
<th>Arterial Blood Gas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>pCO₂, mmHg</td>
</tr>
<tr>
<td>Control group (n = 6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td>28</td>
<td>M</td>
<td>1.84</td>
<td>Chest pain syndrome</td>
<td>82</td>
</tr>
<tr>
<td>C2</td>
<td>31</td>
<td>M</td>
<td>1.50</td>
<td>Chest pain syndrome</td>
<td>80</td>
</tr>
<tr>
<td>C3</td>
<td>15</td>
<td>F</td>
<td>1.50</td>
<td>Functional murmur</td>
<td>76</td>
</tr>
<tr>
<td>C4</td>
<td>42</td>
<td>M</td>
<td>1.74</td>
<td>IHD</td>
<td>76</td>
</tr>
<tr>
<td>C5</td>
<td>20</td>
<td>F</td>
<td>1.48</td>
<td>Small MR</td>
<td>80</td>
</tr>
<tr>
<td>C6</td>
<td>44</td>
<td>F</td>
<td>1.36</td>
<td>Small AR</td>
<td>73</td>
</tr>
<tr>
<td>Mean</td>
<td>30</td>
<td></td>
<td>1.57</td>
<td></td>
<td>78†</td>
</tr>
<tr>
<td>SEM</td>
<td>5</td>
<td></td>
<td>0.07</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>PVH group (n = 8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PV1</td>
<td>25</td>
<td>F</td>
<td>1.35</td>
<td>MS</td>
<td>84</td>
</tr>
<tr>
<td>PV2</td>
<td>30</td>
<td>F</td>
<td>1.50</td>
<td>MS</td>
<td>79</td>
</tr>
<tr>
<td>PV3</td>
<td>37</td>
<td>F</td>
<td>1.70</td>
<td>MS</td>
<td>82</td>
</tr>
<tr>
<td>PV4</td>
<td>31</td>
<td>F</td>
<td>1.44</td>
<td>MS</td>
<td>73</td>
</tr>
<tr>
<td>PV5</td>
<td>55</td>
<td>F</td>
<td>1.46</td>
<td>MS</td>
<td>73</td>
</tr>
<tr>
<td>PV6</td>
<td>42</td>
<td>F</td>
<td>1.44</td>
<td>MS</td>
<td>82</td>
</tr>
<tr>
<td>PV7</td>
<td>46</td>
<td>F</td>
<td>1.80</td>
<td>MS</td>
<td>74</td>
</tr>
<tr>
<td>PV8</td>
<td>36</td>
<td>F</td>
<td>1.25</td>
<td>MS + MR</td>
<td>74</td>
</tr>
<tr>
<td>Mean</td>
<td>38</td>
<td></td>
<td>1.49</td>
<td></td>
<td>78†</td>
</tr>
<tr>
<td>SEM</td>
<td>3</td>
<td></td>
<td>0.06</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>PAH group (n = 10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA1</td>
<td>37</td>
<td>F</td>
<td>1.20</td>
<td>PPH</td>
<td>81</td>
</tr>
<tr>
<td>PA2</td>
<td>30</td>
<td>F</td>
<td>1.48</td>
<td>PPH</td>
<td>63</td>
</tr>
<tr>
<td>PA3</td>
<td>47</td>
<td>F</td>
<td>1.41</td>
<td>Pulm tbc</td>
<td>61</td>
</tr>
<tr>
<td>PA4</td>
<td>40</td>
<td>M</td>
<td>1.55</td>
<td>Pulm tbc</td>
<td>78</td>
</tr>
<tr>
<td>PA5</td>
<td>14</td>
<td>M</td>
<td>1.44</td>
<td>COLD</td>
<td>50</td>
</tr>
<tr>
<td>PA6</td>
<td>49</td>
<td>F</td>
<td>1.42</td>
<td>ASD</td>
<td>63</td>
</tr>
<tr>
<td>PA7</td>
<td>38</td>
<td>F</td>
<td>1.50</td>
<td>ASD</td>
<td>70</td>
</tr>
<tr>
<td>PA8</td>
<td>54</td>
<td>F</td>
<td>1.46</td>
<td>ASD</td>
<td>71</td>
</tr>
<tr>
<td>PA9</td>
<td>50</td>
<td>M</td>
<td>1.46</td>
<td>ASD</td>
<td>64</td>
</tr>
<tr>
<td>PA10</td>
<td>58</td>
<td>M</td>
<td>1.55</td>
<td>ASD</td>
<td>65</td>
</tr>
<tr>
<td>Mean</td>
<td>42</td>
<td></td>
<td>1.43</td>
<td></td>
<td>67</td>
</tr>
<tr>
<td>SEM</td>
<td>4</td>
<td></td>
<td>0.03</td>
<td></td>
<td>3</td>
</tr>
</tbody>
</table>

*SEM = standard error of the mean; IHD = ischemic heart disease; MR = mitral regurgitation; AR = aortic regurgitation; MS = mitral stenosis; PPH = primary pulmonary hypertension; Pulm tbc = pulmonary tuberculosis; COLD = chronic obstructive lung disease; ASD = atrial septal defect.

†p<0.05, compared with the mean value of PAH group.

Baseline of zero velocity on the late diastole. Because the blood flow velocity profile in the pulmonary trunk was reported to be relatively flat, the product of measured velocity and the vessel cross-sectional area expresses the volume of blood flow per unit time. Therefore, if the vessel cross-sectional area is assumed to be constant, the velocity signal would be the same as the volume flow signal. On this assumption, we calculated the mean output signal of the flowmeter in cubic centimeters per second according to the simultaneous pulmonary blood flow measurements by the indicator dilution method. Thus, indocyanine green dye was injected into the pulmonary artery, and the dye dilution curve was recorded in the descending aorta by a catheter. In cases with atrial septal defect (ASD), the dye was injected into the right atrium with a sampling from the pulmonary artery in order to correctly differentiate the shunt flow from the pulmonary blood flow. Using a low resistance flutter valve, a mouth piece, and a nose clip, all patients were asked to breathe air first while their hemodynamic parameters were being recorded. Two 10-ml blood specimens were withdrawn simultaneously from the aorta and from the pulmonary artery for analyses of blood gases and plasma norepinephrine (NE) levels. Then, the patients began to breathe high concentrations of oxygen stored in a Douglas bag. After 10 minutes of the oxygen inhalation, hemodynamic measurements and blood sampling were repeated for each patient. The plasma NE assay was performed according to Renzini's original modified THI method within a fortnight after the blood sampling.

**Calculations and Statistical Analysis**

Details of the technical characteristics of the velocity sensor, including frequency response and drift characteristics, have been described by Murgio. Briefly, the flow velocity probe was used in conjunction with a flowmeter (Narco Bio-System, RT 500). The frequency response of the flow velocity measurements was -3dB at 32 Hz, and the phase shift was linear with the frequency. At least ten consecutive pressure and velocity waves over two respiratory cycles were recorded on magnetic tape (Sony, FE 3907 W) and later digitized at a sample of 5 msec by an analog to digital converter coupled with a minicomputer (Oki, OKITAC-4300C). Then each of those waves was converted to a Fourier series. The impedance modulus was calculated for each harmonic by dividing pressure amplitude by flow amplitude, and the impedance phase by subtracting the flow phase angle from the pressure phase angle. The final average impedance moduli and impedance phase were obtained from those calculations.

Impedance moduli are known to oscillate around the characteristic impedance (Zo) of the proximal vessels. In this study, we
calculated the characteristic value of the proximal arteries by dynes/sec/cm⁵ as the arithmetic mean of impedance moduli between 2 and 10 Hz. Total external power of the right ventricle was also calculated as described in the method by Mihor et al for the mean and pulsatile components of potential and kinetic power (milliwatts) which can be converted to the units of minute work (ergs) and normalized for total blood flow (erg/ml). Pulmonary arterial resistance (PAR) and systemic vascular resistance (SVR) were calculated by dividing the PAP—PCWP difference by the pulmonary blood flow and the mean aortic pressure by the systemic blood flow, respectively.

All statistical analyses were performed by the Student’s paired and unpaired t tests. Differences were considered statistically significant when p values were <0.05. The mean values are expressed in terms of the mean ± SEM.

RESULTS

Inhalation of a high-oxygen concentration increased arterial Po₂ from 78±1 to 434±53 mm Hg in the control group, from 78±2 to 403±23 mm Hg in the PVH group and from 67±3 to 370±33 mm Hg in the PAH group. These values with air breathing were significantly lower in the PAH group than in the PVH and control groups (p<0.05 and p<0.05, respectively). However, these values during oxygen breathing were not significantly different in all three groups. The Po₂ in pulmonary arterial blood also increased from 40±1 to 42±5 mm Hg in the control group and from 36±1 to 43±2 mm Hg in the PVH group. In the PAH group, this value increased from 38±2 to 49±2 mm Hg in five cases without intracardiac shunt diseases and from 50±2 to 101±4 mm Hg in five cases with ASD. The PCO₂ and pH in both arterial and pulmonary blood did not differ significantly due to oxygen breathing in any of the three groups.

The standard hemodynamics during air breathing and oxygen inhalation are shown in Table 2. Oxygen administration decreased heart rate in the two groups

![Table 2—Hemodynamic Parameters Before and During Oxygen Breathing*](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21346/)
In the control group, the modulus before oxygen breathing fell steeply from zero frequency to the first harmonic which occurred at 1 to 3 Hz. Oxygen administration did not cause any change in the impedance spectra. In the PVH group, the moduli did not lower during oxygen breathing either, although the modulus at zero frequency lowered in all but one case. In the PAH group, the impedance spectra showed a different pattern between the five cases without intracardiac shunt diseases which had high impedance moduli and the five cases with ASD which had relatively low moduli. Oxygen administration caused the impedance moduli to decrease in both cases, thereby shifting the impedance curve downward. When we calculated Zo from these moduli, rises and falls in the Zo were found with oxygen breathing in the control and PVH groups, and there was no significant overall change (Fig 2). In contrast, Zo significantly decreased from 78 ± 18 to 57 ± 14 dynes·sec·cm⁻² in all the cases in the PAH group (p < 0.01). In this group, the frequency at which the first minimum of the impedance modulus occurs (f₀) also decreased from 4.7 ± 0.7 to 4.0 ± 0.6 Hz in all the cases but one; however, the decrease was not statistically significant.

Both mean and pulsatile components of the right ventricular minute work index (erg·min⁻¹/m²) significantly decreased from 12.9 ± 2.0 and 3.2 ± 0.7 to 10.2 ± 1.7 and 2.4 ± 1.1 in the PVH group (p < 0.01 and p < 0.05, respectively), and from 24.9 ± 3.3 and 9.1 ± 1.4 to 22.6 ± 3.3 and 7.9 ± 1.3 in the PAH group (p < 0.01 and p < 0.05, respectively.) In the control group, the mean work decreased from 8.2 ± 0.8 to 6.0 ± 0.5 (p < 0.05), but the reduction in the pulsatile work was not significant (4.3 ± 0.8 to 3.8 ± 0.8). When we normalized those works for individual total blood flow, mean work decreased in all the groups, but the reduction of the pulsatile work was only observed in the PAH group (from 2.0 ± 0.5 to 1.6 ± 0.4 erg·min⁻¹/m²).

The input impedance spectra before and during oxygen breathing are summarized in Figure 1. In the control group, the modulus before oxygen breathing fell steeply from zero frequency to the first harmonic which occurred at 1 to 3 Hz. Oxygen administration did not cause any change in the impedance spectra. In the PVH group, the moduli did not lower during oxygen breathing either, although the modulus at zero frequency lowered in all but one case. In the PAH group, the impedance spectra showed a different pattern between the five cases without intracardiac shunt diseases which had high impedance moduli and the five cases with ASD which had relatively low moduli. Oxygen administration caused the impedance moduli to decrease in both cases, thereby shifting the impedance curve downward. When we calculated Zo from these moduli, rises and falls in the Zo were found with oxygen breathing in the control and PVH groups, and there was no significant overall change (Fig 2). In contrast, Zo significantly decreased from 78 ± 18 to 57 ± 14 dynes·sec·cm⁻² in all the cases in the PAH group (p < 0.01). In this group, the frequency at which the first minimum of the impedance modulus occurs (f₀) also decreased from 4.7 ± 0.7 to 4.0 ± 0.6 Hz in all the cases but one; however, the decrease was not statistically significant.

Both mean and pulsatile components of the right ventricular minute work index (erg·min⁻¹/m²) significantly decreased from 12.9 ± 2.0 and 3.2 ± 0.7 to 10.2 ± 1.7 and 2.4 ± 1.1 in the PVH group (p < 0.01 and p < 0.05, respectively), and from 24.9 ± 3.3 and 9.1 ± 1.4 to 22.6 ± 3.3 and 7.9 ± 1.3 in the PAH group (p < 0.01 and p < 0.05, respectively.) In the control group, the mean work decreased from 8.2 ± 0.8 to 6.0 ± 0.5 (p < 0.05), but the reduction in the pulsatile work was not significant (4.3 ± 0.8 to 3.8 ± 0.8). When we normalized those works for individual total blood flow, mean work decreased in all the groups, but the reduction of the pulsatile work was only observed in the PAH group (from 2.0 ± 0.5 to 1.6 ± 0.4 erg·min⁻¹/m²).
Although the PAH group studied here consisted of patients with a variety of diseases, breathing oxygen decreased PAR in all cases in this group. This indicates that their pulmonary vascular beds remain labile to oxygen stimulation. In contrast, this resistance showed no significant overall change in the pulmonary vessels of the PVH group, which suggests that there is little space for oxygen. The response of standard hemodynamics to hyperoxia was almost compatible with previous reports including subjects with and without pulmonary hypertension.\(^1\)\(^-\)\(^7\)\(^8\) Of these responses, the increase in SVR seems to be an interesting phenomenon, since the direction of the response is completely opposite to that of PAR. As shown in Table 2, SVR increased in all the groups, although the increase in SVR in the PAH group was not significant. Exceptional cases in the PAH group were found in two patients with primary pulmonary hypertension and in one case with chronic obstructive lung disease. It is probable that in these cases the oxygen effect on PAR is far more striking than on SVR.

Effects of Oxygen Breathing on Pulmonary Vascular Impedance

Our major concern is to understand how oxygen breathing changes the stiffness of the large pulmonary arteries in pulmonary hypertensive patients. It is well-known that stiffening of the conduct vessels tends to augment pressure pulsation and increases the opposition to pulsatile flow.\(^2\)\(^-\)\(^8\) The opposition to pulsatile flow could be represented as the ratio of the pressure modulus to the flow modulus for each of an integral number of harmonics and expressed in terms of fluid impedance. Therefore, if hyperoxia induces either an increase or a decrease in stiffness of the proximal pulmonary arteries, this will change the input impedance spectra in those vessels. Recent advances in the catheter-tip velocity transducer have made it possible to record the pulsatile flow in the pulmonary vessels of

**DISCUSSION**

**Effects of Oxygen Breathing on Standard Hemodynamics**

**Figure 3.** Changes of right ventricular minute work normalized for total blood flow during oxygen breathing in three groups. Upper panel, pulsatile component; lower panel, mean component of minute work.

10\(^8\)/ml, \(p<0.01\) (Fig 3).

During air breathing, plasma arterial NE levels were significantly higher in the PAH group than in the control group (\(p<0.05\)). Plasma arterial NE levels did not change in the control and PVH groups due to oxygen breathing, while there was a slight but significant decrease in the PAH group (381 ± 89 to 319 ± 77 pg/ml, \(p<0.01\)) (Fig 4). Similar reduction was observed in pulmonary arterial plasma NE levels in the PAH group, although significant NE extraction by the lung had been reported.\(^2\) A significant correlation was found between the percent change in Zo and that in NE in arterial blood in individual patients (Fig 5).

**Figure 4.** Changes of plasma arterial norepinephrine (NE) levels in three groups during oxygen breathing.
Oxygen inhalation caused the reduction in the impedance moduli and shifted the curve downward in all cases in the PAH group. However, such changes were not found in the PVH group and the control group. The reduction in impedance moduli in the PAH group is a considerably important factor in reducing right ventricular afterload, because the opposition to pulsatile flow in pulmonary arteries accounts for a highly significant portion of the total hydraulic power generated by the right ventricle.

Since the hemodynamic effects of oxygen breathing on the pulmonary circulation have been evaluated only with mean hemodynamic values, it is still unknown how the pulsatile work changes. In calculating the external right ventricular work, it was found that oxygen caused a reduction in pulsatile work as well as mean work in the groups with pulmonary hypertension. Since the flow is the major determinant of the magnitude of the external work, we normalized the work for individual total blood flow. As shown in Figure 3, the reduction in the normalized pulsatile work was only observed in the PAH group.

This reduction in the pulsatile work might be partly due to a decrease in wave reflection which would affect the f_{\text{ave}}. However, we could not find any substantial evidence about the changes in wave reflection. In contrast, we could find a significant change in Zo in the PAH group. It is generally accepted that this index represents the elastic properties of the vascular wall and thus is associated with the alterations in impedance moduli. In other words, the increased Zo implies a less distensible vessel. This index assumed to be less dependent on the possible effect of intravascular pressure itself, although the elastic modulus of the vascular wall changes as the strain changes. Therefore, the increase or the decrease in Zo seems to be analogous to a stress-strain curve shifting either to the left and upward or to the right and downward. As shown in Figure 2, the Zo apparently decreased in all the cases in the PAH group. These results lead to the conclusion that oxygen breathing can decrease the stiffness of the proximal pulmonary arteries in the PAH group.

Possible Mechanism of Reduction in Zo During Oxygen Breathing

The question arises then as to what mechanism is responsible for the change in Zo in the PAH group but not in the PVH or control group during oxygen breathing. One might assume that the large pulmonary artery's response to hyperoxia is similar to that of the small pulmonary artery. However, even high oxygen in alveoli will not directly reach the main pulmonary arteries so that the diffusive effect of oxygen cannot be expected in those vessels. This change cannot be explained by differences in oxygen tension in blood.
either, because both arterial and pulmonary arterial 
P_02 were similarly elevated by oxygen breathing in all 
three groups. The P_02 in the pulmonary arterial blood 
of patients with ASD was already high during the 
control period. But oxygen breathing decreased the Zo 
as well as the Zo of five other cases in the PAH group. 
Another possibility is that the reduction in Zo resulted 
from the increased wall distensibility due to the 
intravascular pressure fall. In this study, we could not 
clarify whether the pressure fall directly affects the 
value of Zo. However, as mentioned above, it has been 
reported that the Zo is less dependent on changes in 
intravascular pressure. According to Womersley’s 
equation, Zo is determined by vascular diameter and 
the elastic properties of the wall. If a pressure fall 
results during oxygen breathing, the vascular diameter 
will decrease, and the increased volume distensibility 
will be counterbalanced. Actually, the Zo did not 
change in the PVH and control groups despite the 
decreased PAP. It is unlikely, therefore, that a fall in 
pulmonary arterial pressure itself induces a reduction 
in Zo.

The most likely mechanism for the reduction in Zo 
seems to be the indirect effect of oxygen on the vessels 
through an attenuation of sympathetic nerve tone. Our 
results demonstrated that the reduction in Zo was 
associated with a decrease in plasma NE levels in the 
PAH group. In contrast, plasma NE did not decrease in 
either the PVH group or the control group, which 
showed no significant change in Zo. As shown in 
Figure 5, a significant correlation was observed be-

tween the reductions in Zo and those in plasma NE 
levels in the aorta in individual patients. There have 
been numerous experimental works which support 
that sympathetic nerve tone can change the wall 
properties of the large pulmonary artery.28-32 Pace33 
found that stimulation of the left stellate ganglion 
increased the impedance modulus of the large pulmo-
nary artery in open chest dogs, while pulmonary 
vascular resistance was less affected. Piene34 reported 
that the pulmonary vascular impedance of cats was 
increased by norepinephrine infusion as well as by 
sympathetic nerve stimulation. Thus, it is also possible 
to assume that if the sympathetic nerve tone returns 
to its baseline during oxygen breathing, the vascular 
stiffness will decrease.

Effects of Oxygen Breathing on Plasma NE Levels

During air breathing, plasma NE levels were higher 
in the PAH group than in the other two groups. This 
might be a reason why oxygen breathing decreased NE 
in only the PAH group, although the cause of the 
increase in NE levels in the PAH group is probably 
multifactorial.35 Watanabe et al.36 found that plasma NE 
levels increased in patients with chronic cor pulmonale 
and thought that those patients were in hyperven-

tilation. The subjects included in our study are somewhat different from 
theirs. However, it is interesting that there is a 
significant difference between arterial P_02 in the PAH 
group and that in the other two groups during air 
breathing. The former group showed a relatively low 
arterial P_02 which had been observed in this disor-
der.34-35 This low arterial P_02 will stimulate the sympa-
thetic nerve system through the carotid and aortic 
chemoreceptors or through metabolites in peripheral 
tissues. Oxygen breathing will immediately correct 
this hypoxemia, and thus the excitability of the sympa-
thetic nerve will be gradually suppressed. Therefore, it 
seems to be very likely that the enhanced tone of the 
sympathetic nerve in the PAH group could be attenu-
ated after the correction of hypoxemia.

All of these observations led us to conclude that 
the intervention of oxygen breathing reduces the pulmo-
nary vascular impedance in the PAH group. This 
reduction could be ascribed to the reduction in Zo 
which indicates the stiffness of the large pulmonary 
arteries. In addition, it was observed that oxygen 
breathing attenuated the sympathetic nerve excitabil-
ity which was found in the PAH group. Thus, it is 
most likely that oxygen reduces the vascular tone of the 
large pulmonary vessels indirectly through the correc-
tion of the sympathetic nerve excitability. As a result of 
that, oxygen breathing could reduce the right 
ventricular load in the PAH group by attenuating the 
pulsatile work as well as the mean work. We believe 
that the present results will provide useful information 
on the beneficial effects of oxygen therapy for patients 
with pulmonary hypertension.

REFERENCES

1 Burchell HB, Swan HJC, Wood EH. Demonstration of differen-
tial effect on pulmonary and systemic arterial pressure by 
variation in oxygen content of inspired air in patients with patent 
ductus arteriosus and pulmonary hypertension. Circulation 
1953; 8:681-94
2 Swan HJC, Burchell HB, Wood EH. Effect of oxygen on 
pulmonary vascular resistance in patients with pulmonary hyper-
tension associated with atrial septal defect. Circulation 1959; 
20:66-73
3 Marshall HW, Swan HJC, Burchell HB, Wood WH. Effect of 
breathing oxygen on pulmonary artery pressure and pulmonary 
vascular resistance in patients with ventricular septal defect. 
Circulation 1961; 23:241-52
4 Krongrad E, Heimholz HF Jr, Ritter DG. Effect of breathing 
oxygen in patients with severe pulmonary vascular obstructive 
5 Morrison G, Macartney F. Effects of oxygen administration, 
bicarbonate infusions, and brief hyperventilation on patients 
with pulmonary vascular obstructive disease. Br Heart J 1979; 
41:584-93
6 Conhaim RL, Staub NC. Reflection spectrophotometric mea-
surement of O2 uptake in pulmonary arteries of cats. J Appl 
Physiol 1980; 48:848-56
7 Daley WJ, Bondurant S. Effects of oxygen breathing on the heart 
rate, blood pressure, and cardiac index of normal men: resting,
with reactive hyperemia, and after atropine. J Clin Invest 1962; 41:126-32
10 McDonald DA. Blood flow in arteries. Baltimore: Williams & Wilkins, 1974
11 Bergel DH, Milnor WR. Pulmonary vascular impedance in the dog. Circ Res 1965; 16:401-15
34 Wessel HU, Kezzi F, Cugell DW. Respiratory and cardiovascular function in patients with severe pulmonary hypertension. Circulation 1964; 29:825-31

Cardiac Imaging Update

The North American Society for Cardiac Radiology will present this course May 9-12 at The Registry Resort, Scottsdale, Arizona. For information, contact: Educational Resources Associates, PO Box 369, Brookline Massachusetts 02146 (617.738-8859).

Third Advanced Cardiovascular Nuclear Medicine Workshop and the AHA Council on Clinical Cardiology

Sponsored by Massachusetts General Hospital, this program will be held April 22-23 at the Massachusetts General Hospital. For information, contact Dr. Kenneth A. McKusick, Course Director, c/o Educational Resources Associates, PO Box 369, Brookline, Massachusetts 02146 (617.738-8859).