Aortic and Pulmonary Input Impedance in Patients with Cor Pulmonale

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Summary

The hydraulic load of the right and left ventricles and the clinical effects of nifedipine were evaluated in 8 normal subjects (mean age: 55 years) and 8 patients with cor pulmonale secondary to chronic obstructive lung disease (mean age: 57 years). It was found that there were differences in the right ventricular resistance (174.62 +25.96 vs 468.57 ± 178.81 dyne/sec/cm^{-5}), first zero crossing frequency (3.62 ± 0.34 vs 6.07 ± 3.56 Hz), steady power (218.95 ± 32.25 vs 359.44 ± 37.46 mW) and total power of right ventricle (275.81 ± 36.18 vs 440.46 ± 85.16 mW) between the normal and cor pulmonale patients, respectively. However, no significant changes in characteristic impedance, pulsatile power or aortic impedance were observed in the right pulmonary artery. After administration of nifedipine to patients with cor pulmonale, there were significant changes in resistance (468.57 ± 178.81 vs 256.36 ± 178.56 dyne/sec/cm ^{5}), steady power (359.44 ± 37.46 vs 225.51 ± 114.64) and total power (440.46 ± 85.16 vs 289.27 ± 50.85) of the pulmonary artery, respectively. Otherwise there were no significant changes in aortic input impedance or characteristic impedance of right pulmonary artery and pulsatile power.

In conclusion, we found that: 1) the hydraulic vascular load in the right ventricle was higher in patients with cor pulmonale, 2) characteristic impedance that was not increased in cor pulmonale patients may be due to a dilated pulmonary artery, 3) there was no impedance mismatch between left ventricle and systemic arterial system in patients with cor pulmonale, and 4) by reducing the pulmonary vascular resistance through nifedipine administration, the total external right ventricular power might be reduced, without affecting the proximal pulmonary arterial compliance.

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VASCULAR input impedance—the ratio of the oscillatory pressure to oscillatory flow at the origin of the pulmonary artery or ascending aorta—provides information about the dynamic properties of the arterial system. In addition, estimates can be made of the hydraulic energy required to move blood into the vascular bed in a pulsatile fashion. Pulmonary vascular and aortic input impedance have been studied in rabbits, dogs and men.[1)-13)] Changes in the elasticity of the pulmonary or systemic arteries significantly alter the impedance spectrum and affect the pulsatile power expenditure. Pulmonary hypertension in man is associated with the increased energy requirement for the movement of blood through the vascular bed, and this work has been characterized by steady flow power calculations based on mean flow and mean pressure, with a corresponding increase in the pulsatile power dissipated in maintaining pulsatile flow.

One of the purposes of this study is to evaluate the hydraulic load of the right ventricle in patients with cor pulmonale secondary to chronic obstructive lung disease. Moreover, since it is unclear whether the left side hemodynamics may be affected by pulmonary hypertension in patients with cor pulmonale, the second purpose is to evaluate the interaction of the left ventricular and aortic vascular systems in patients with cor pulmonale.

Over the past 20 years a number of vasodilator drugs have been administered to patients with pulmonary hypertension.[14)-20)] However, the utility of calcium channel blockade in the treatment of pulmonary hypertension and other obliterative pulmonary vascular diseases is controversial.[21)-24)] Thus, the third purpose of this study is to determine the mechanism and magnitude of right vascular unloading during administration of nifedipine in patients with cor pulmonale so as to assess whether this agent possesses a primary effect on right ventricular load through a direct effect on pulmonary vascular resistance and impedance.

Materials and Methods

Patients and data acquisition:

Eight patients with stable cor pulmonale secondary to chronic obstructive lung disease were classified as having one of the three types of ventilatory defects: obstruction, restriction or limited obstruction and restriction. None of these patients had a history of myocardial infarction or coronary artery

disease. None had valvular heart disease or clinical left ventricular failure. Informed consent was obtained from all patients.

All patients underwent routine pulmonary function studies during their stable period. They all had electrocardiographic findings of right ventricular hypertrophy. Treatment with bronchodilators and diuretic drugs was discontinued before the day of the study.

Hemodynamic measurement:

Right and left heart catheterization was performed on the 16 subjects percutaneously via the femoral vein and artery, respectively. Diagnostic catheterization was performed first to rule out coronary heart disease and other valvular heart diseases. Then the standard catheters were replaced by a specially designed high fidelity catheter (Millar Instrument Co., Med Right side VPC 673-A, Left side SD 156, SN 131). The 7F left heart catheter had two pressure transducers, located 1 and 6 cm from the tip. In addition, an electromagnetic flow velocity sensor was located 2 cm distal to the second pressure sensor. The 7F right heart catheter also had two pressure transducers, located 1 and 12 cm from the tip, and an electromagnetic flow velocity sensor located another 5 cm distal to the second pressure sensor. The velocity sensor was connected to a Biotronex BL 610 flowmeter. The flow system had a frequency response that decreased 3 Db at about 75 Hz. The left heart catheter was advanced retrogradely across the aortic valve to help stabilize the catheter and center the sensors in the stream, while allowing simultaneous measurement of left ventricular pressure, ascending aortic pressure and flow velocity. The right heart catheter was placed across the pulmonary valve to the pulmonary artery, allowing simultaneous measurement of right ventricular pressure, pulmonary artery pressure and flow velocity.

The catheter was manipulated to obtain an optimal flow velocity signal, characterized by a steady diagnostic level with maximal systolic amplitude and minimal late systolic negative flow. The pressure and flow velocity signals were displayed with a 6-channel Hewlett-Packard monitor and a strip-chart recorder, and were recorded simultaneously on tape (Hewlett-Packard #3968A). The pulmonary artery and ascending aortic cross sectional areas were obtained from two-dimensional echocardiogram. To minimize drift before inserting each catheter, the sensors were soaked and prewarmed for at least 3 hours at 37° centigrade in saline. After withdrawing each catheter, it was reimmersed in the bath to check for baseline drift.

Baseline resting hemodynamics were recorded first in both groups. Then nifedipine (10 mg sublingually) was given to patients with cor pulmonale. After 15–20 min, when the systolic blood pressure declined by 10 mm-

Hg, hemodynamics measurements were repeated.

Data analysis:

All data were recorded on magnetic tape, using a Houston Instrument true GRIDth digitizer. Five cardiac cycles were selected for analysis from each intervention. The pressure and flow signals obtained from the high-fidelity micromanometer catheter were computed and resolved into their Fourier harmonics, based on Fourier analysis of the pressure and flow waveforms.[25] The following parameters were analyzed: 1) The input impedance was calculated as the ratio of the pressure to flow moduli. The corresponding phase angle was derived by subtracting the flow phase angle from the pressure phase angle. 2) The characteristic impedance was taken as the average impedance modulus between 2 and 12 Hz. 3) The wave reflections of each vascular bed were assessed by calculating the difference between the maximum and minimum impedance moduli and by estimating the first zero crossing of the phase angle, which was obtained by linear interpolation.[26] 4) The velocity of blood flow was estimated by the Womersley equation,[27] using the pressure differential that was recorded by the two pressure transducers of the high-fidelity micromanometer catheter. 5) The resistance of each vascular bed was calculated by subtracting the estimated mean atrial pressure from the mean arterial pressure and dividing by mean flow. The mean atrial pressure was estimated by the time average of ventricular pressure from the point of atrioventricular valve opening (obtained from two-dimensional echocardiogram) until end-diastole.

The hydraulic power was calculated as described by Milnor.[26] Steady flow power was calculated as the product of the mean pressure and mean flow. Pulsatile power was computed directly from the Fourier harmonics. The total power was the sum of steady flow and pulsatile power.

Statistical analysis:

All reported data are presented as mean±SD, a paired t-test was used to assess changes within individuals and an unpaired t-test was used for group comparisons. A p value less than 0.05 was considered statistically significant.

Results

The hemodynamic data for the normal and patient groups are listed in Tables I and II. The 2 groups did not differ in age, height, body weight or aortic diameter, but pulmonary arterial diameter was greater in the patient group ($p<0.01$). The systemic systolic, diastolic and mean aortic pressures

also presented no differences. However, the pulmonary systolic, diastolic and mean pulmonary arterial pressure were higher in patients with cor pulmonale ($p<0.001$), and their heart rates also tended to be higher. After nifedipine administration, the hemodynamics including systemic systolic pressure, pulmonary systolic pressure and mean pulmonary pressure were significantly changed. However, the changes were not accompanied by significant changes in heart rate, mean pulmonary or systolic flow, aortic, diastolic or mean pressure.

The mean values of impedance and power parameters are summarized in Tables I and II. The impedance spectrum of mean values for normal subjects and each cor pulmonale patient are shown in Figs. 1 and 2. The impedance fell rapidly from a relatively high value at zero frequency to a minimum between 4 and 6 cycles in patients with cor pulmonale. After nifedipine administration the pulmonary vascular resistance was significantly decreased, but there were no changes in characteristic impedance and first zero crossing. The aortic impedance did not differ significantly between the 2 groups, even after nifedipine (Table II).

The steady power was higher in patients with cor pulmonale than in normal subjects (Table I). However, the pulsatile power was unchanged. Thus, the total power was higher in cor pulmonale patients because of increased steady power. After nifedipine administration, the steady and total power were significantly reduced, but there was no change in pulsatile power.

Discussion

Pulmonary input impedance:

The input impedance spectrum of normal subjects in the main pulmonary artery is consistent with other reports.[8),28)] The pulmonary arterial input impedance spectrum, like that of the ascending aorta, fell steeply from a relatively high value at zero frequency to a minimum at 2–4 Hz, followed by a relative maximum at 6–8 Hz. The characteristic impedance of the main pulmonary artery was 33.79 ± 5.03 dyne/sec/cm ^{5}, which is in agreement with other reports.[8),28)] This impedance is lower than that of the aorta, which probably reflects a lower elastic modulus and peripheral resistance. In patients with cor pulmonale, the pulmonary input impedance displayed both increased resistance and a shift to the right of the first minimum of impedance. The shift of impedance suggests that there is a more proximal location of the wave reflective site in pulmonary arteries than in normal subjects.

The characteristic impedance was not increased, as described in other reports of pulmonary hypertension. It appears that the increase in charac-

Table I. Right Side Hemodynamic Data in Normal Subjects

		Age (yrs)	PSP (mmHg)	PDP (mmHg)	MP (mmHg)	PF (ml/sec)
NC	mean	54.00	26.63	12.13	19.26	84.19
	SD	±6.73	±2.50	±1.84	±2.59	±6.83
	p value	NS	<0.001	<0.001	<0.001	NS
	vs. CP without treatment					
CP without treatment	mean	58.20	49.61	25.37	35.42	75.57
	SD	±5.30	±14.07	±6.26	±8.74	±19.92
	p value		<0.001	<0.05	<0.01	NS
	vs. CP with nifedipine					
CP with nifedipine	mean	58.20	35.88	18.71	22.34	74.27
	SD	±5.30	±12.42	±6.69	±8.54	±27.87

NC = normal control; CP = cor pulmonale; PSP = pulmonary systolic pressure; MP = mean pulmonary pressure; PF = pulmonary flow; PA = pulmonary artery diameter; R = resistance; Zl = first har-

Table II. Left Side Hemodynamic Data in Normal Subjects and

		HR (beats)	SP (mmHg)	DP (mmHg)	P (mmHg)	Ao (cm^2)	F (ml/sec)
NC	mean	78.01	125.49	75.24	99.54	2.73	90.63
	SD	±12.2	±12.38	±8.12	±9.27	±0.37	±31.06
	p value	<0.05	NS	NS	NS	NS	NS
CP without treatment	mean	94.31	126.30	77.99	99.06	2.47	69.84
	SD	±13.24	±22.41	±12.36	±16.86	±0.36	±31.96
	p value	NS	<0.05	NS	NS	NS	NS
CP with nifedipine	mean	98.38	115.19	73.77	94.36		72.43
	SD	±16.12	±23.84	±11.40	±17.35		±12.48

NC = normal control; CP = cor pulmonale; SP = systolic pressure; DP = diastolic pressure; P = mean aortic pressure; Ao = aortic diameter; F = mean aortic flow; R = resistance; Zl = first harmonic im-

teristic impedance in other studies could be the result of a passive decrease in pulmonary artery compliance (defined as the change in volume per unit pressure in the pulmonary artery), resulting from the increased distension pressure or an actual histologic change.[29)-32)] This was, however, not found in the present study. This may reflect dilatation of the cross-sectional area or main pulmonary artery (PA diameter 2.4 cm^2 vs normal 1.98 cm^2, $p < 0.001$), since the characteristic impedance is inversely related to the cross-sectional area of the vessel.[26)]

and in Patients with Cor Pulmonale Before and After Nifedipine

PA (cm^2)	Total (mW)	Steady (mW)	Pulsatile (mW)	R (dyne-sec-cm $^{-5}$)	Zl (dyne-sec-cm $^{-5}$)	Zc (dyne-sec-cm $^{-5}$)	Fo (Hz)
1.98	275.81	218.95	56.87	174.62	49.36	33.79	3.62
±0.06	±36.18	±32.25	±6.11	±25.96	±8.90	±5.03	±0.34
<0.001	<0.001	<0.001	NS	<0.05	<0.01	NS	<0.05
2.40	440.46	359.44	81.12	468.57	168.74	58.69	6.07
±0.02	±85.16	±37.46	±60.46	±178.81	±123.09	±52.03	±3.56
<0.01	<0.05	<0.05	NS	<0.01	NS	NS	NS
	289.27	225.51	65.02	256.36	123.30	45.72	4.48
	±50.85	±114.64	±39.38	±178.56	±81.56	±22.91	±2.05

monic impedance; Zc=characteristic impedance; Fo=first zero crossing.

in Patients with Cor Pulmonale Before and After Nifedipine

Total (mW)	Steady (mW)	Pulsatile (mW)	R (dyne-sec-cm $^{-5}$)	Zl (dyne-sec-cm $^{-5}$)	Zc (dyne-sec-cm $^{-5}$)	Fo (Hz)
1427.94	1221.40	206.50	1572.06	245.67	134.63	3.12
±542.73	±513.90	±49.33	±396.05	±32.80	±52.35	±0.94
NS	NS	NS	NS	NS	NS	NS
1242.11	1041.37	200.74	1803.27	253.54	154.19	3.92
±574.81	±480.04	±96.64	±335.98	±38.69	±48.80	±1.91
NS	NS	NS	NS	NS	NS	NS
1013.27	867.77	132.64	1908.05	242.00	167.11	4.12
±324.50	±280.02	±69.91	±466.96	±36.02	±102.55	±1.91

pedance; Zc=characteristic impedance; Fo=first zero crossing.

Aortic input impedance:

The input impedance of the ascending aorta has been measured repeatedly in men as well as in dogs.[2),5),11)] The complex relationship between pulsatile pressure and pulsatile flow in the ascending aorta provides a measure of the dynamic physical properties of the arterial tree. This function considers not only the relationship of mean pressure and mean flow but also the elasticity of the aortic wall, inertial properties of the blood and the effects of wave reflection. Clinically, an increased resistance and characteristic impedance have produced an elevated pressure during systole, which may lead to increases in total heart work and myocardial oxygen consumption. These

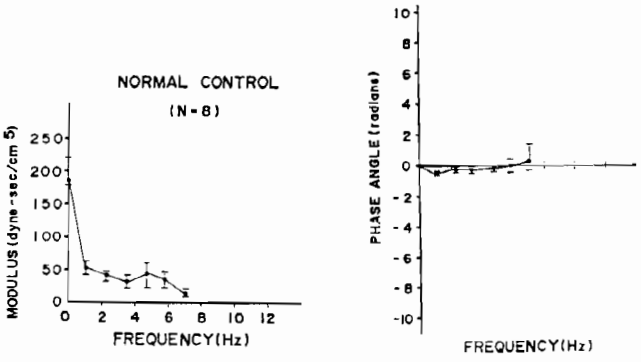

Fig. 1. Averaged pulmonary input impedance spectra in 8 normal subjects. Modulus (left), phase angle (right).

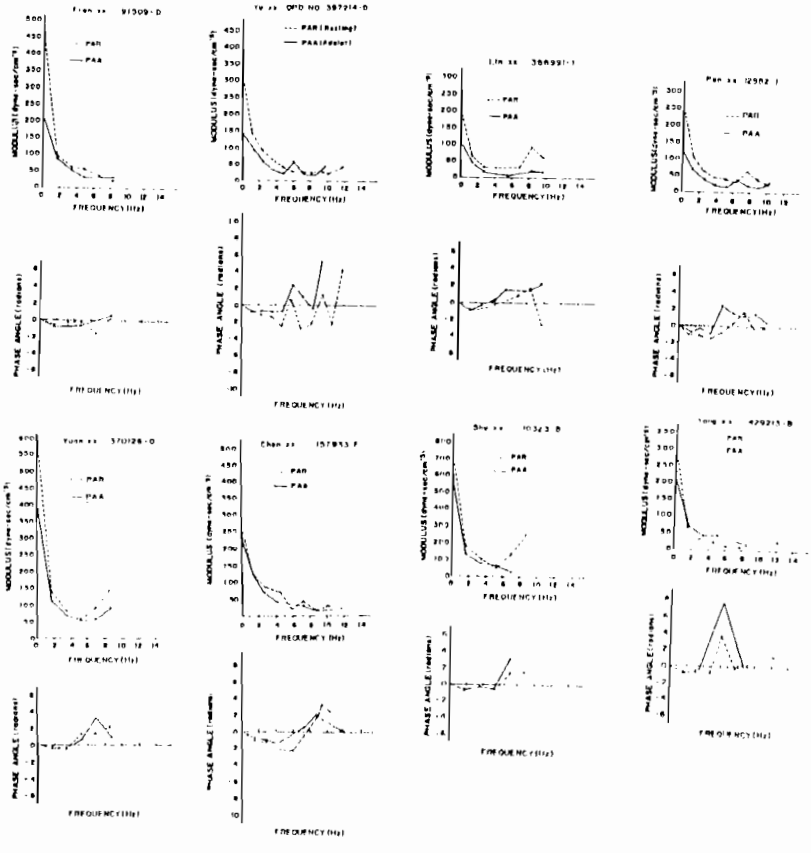

Fig. 2. Pulmonary input impedance spectra in the 8 patients with cor pulmonale. PAR = pulmonary arterial impedance during resting stage; PAA = pulmonary arterial impedance after adalat (nifedipine).

changes, then, can impair ventricular ejection and induce ventricular dysfunction.

In vivo studies[32) 35)] have shown that the structure and function of the left ventricle can be abnormal as a result of the pathological mechanisms underlying cor pulmonale, even though the usual etiologies of left ventricular disease were not apparent. In our patients with cor pulmonale, though, the aortic input impedance was similar to normal subjects. The hydraulic power was also not increased. This implies that although the patients had been in a long-standing hypoxic state, an impedance mismatch between the left ventricle and systemic arterial system was not apparent in our cor pulmonale patients. This leads to the speculation that in patients with cor pulmonale without associated diseases such as coronary artery diseases, left ventricular dysfunction may not be responsible for the pathological mechanism underlying cor pulmonale.

Hydraulic power:

The hydraulic power (or work per unit time) associated with blood flow at the root of the aorta or pulmonary artery depends upon both the ability of the left or right ventricle to do external work, and the properties of the arterial tree into which blood is ejected. Aortic or pulmonary input impedance is an expression of these properties. The steady power represents energy loss in maintaining steady flow through small resistance vessels, while pulsatile power represents energy lost in the arterial system as a consequence of intermittent ventricular ejection. The relatively high total hydraulic power in our patients with cor pulmonale may thus indicate an increase in the steady power or pulsatile power, or both. Since the pulsatile power was not increased in this study, the increase in total hydraulic power in patients with cor pulmonale was mainly due to peripheral resistance.

Experimental studies have shown that calcium channel blockade inhibited the pulmonary vasoconstrictor response to acute hypoxia and reduced the severity of both pulmonary hypertension and secondary right ventricular hypertrophy induced by chronic hypoxia.[21)] Moreover, hypoxia appears to induce pulmonary hypertension by interrupting the ability of arterial smooth muscle cells to maintain a transmembrane ionic gradient.[21)] The resultant increase in cytoplasmic calcium levels leads to pulmonary arterial constriction that can be blocked by calcium antagonists. In a majority of clinical studies,[22),23)] nifedipine increases cardiac output, decreases pulmonary artery pressure and pulmonary vascular resistance, and improves right ventricular function. In our study, pulmonary artery pressure and pulmonary vascular resistance were significantly decreased after nifedipine administration. The

hydraulic load of the right ventricle was also reduced through a decrease in the steady power. Since there was no change in the pulsatile power, the proximal pulmonary arterial compliance was not affected by nifedipine administration.

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