Effects of Pacing Tachycardia and Balloon Valvuloplasty on Pulmonary Artery Impedance and Hydraulic Power in Mitral Stenosis

William G. Kussmaul III, MD; Jonathan A. Altschuler, MD;
Howard C. Herrmann, MD; and Warren K. Laskey, MD

Background. **Mitral stenosis is characterized by progressive pulmonary hypertension and eventual right ventricular failure. However, the correlation between right ventricular failure and the level of pulmonary hypertension is poor, suggesting that factors other than those recognized from nonpulsatile hemodynamic parameters may contribute to impaired right ventricular performance in this condition.**

Methods and Results. **We studied 16 patients with severe mitral stenosis (mean valve area, 1.0±0.2 cm^2) at supine rest and during pacing tachycardia using high-fidelity catheter recordings of pulmonary artery (PA) pressure and flow velocity. Pulmonary impedance spectra, wave reflection properties, and hydraulic power data were derived from Fourier analysis of signal-averaged data. Pacing tachycardia (baseline heart rate, 81±11 beats per minute; pacing, 132±11 beats per minute) significantly raised pulmonary wedge and mean PA pressures. There was no change in pulmonary vascular resistance (209±144 to 232±164 dyne-sec/cm^5) or PA characteristic impedance (62±25 to 55±28 dyne-sec/cm^5). However, first harmonic impedance (Z_1) significantly decreased (134±71 to 100±68 dyne-sec/cm^5; $p<0.001$). Accordingly, oscillatory and total dissipated hydraulic power per unit forward flow (W_T/CO) fell during tachycardia (2.6±1.6 to 2.3±1.4 mW/ml · sec^{-1}; $p=0.06$) despite acute pulmonary hypertension. Reflected pressure waves returned earlier to the proximal PA, suggesting increased vessel stiffness. Immediately after percutaneous balloon mitral valvuloplasty (PBV) in eight of the patients, baseline and pacing data were again recorded. Compared with the pre-PBV baseline state, post-PBV resting data demonstrated no change in resistance or characteristic impedance, but there was a significant fall in Z_1 (166±75 to 103±45 dyne-sec/cm^5; $p<0.05$) and in the magnitude of pulmonary wave reflections. W_T/CO tended to decrease after PBV, and pacing after PBV produced a further decrease in W_T/CO, again in association with lower Z_1.**

Conclusions. **These data demonstrate that 1) increased pulmonary characteristic impedance, although a feature of mitral stenosis, is not exacerbated by the acute effects of increased distending pressure; 2) pacing tachycardia in mitral stenosis causes little change in the pulmonary impedance spectrum except at low frequencies, where decreased impedance lowers power requirements per unit flow; and 3) relief of mitral stenosis produces immediate improvement in low-frequency impedance and in hydraulic power requirements. These findings suggest that although characteristic impedance may be a measure of the long-term effects of pulmonary hypertension on the pulmonary circulation, acute increases and decreases in PA pressure produce effects on right ventricular load that are best described in terms of the low-frequency properties of the PA system. Improvement in low-frequency impedance diminishes hydraulic power requirements and thus reflects improved ventricular-vascular coupling, irrespective of distending PA pressure. Efforts to treat or prevent right heart failure in the presence of pulmonary hypertension should take account of the potential benefit of changes in low-frequency impedance characteristics of the pulmonary vascular bed. (*Circulation* 1992;86:1770–1779)**

KEY WORDS • **pulmonary hypertension** • **wave reflection** • **balloons** • **valvuloplasty** • **tachycardia** • **pacing** • **mitral stenosis**

Mitral stenosis is characterized by chronically increased left atrial and pulmonary pressures, leading eventually to right ventricular dilation and failure. Tachycardia has been shown to produce further pressure elevation as a result of a shorter left ventricular diastolic filling period, contributing to exertional symptoms.[1,2] However, the mechanisms by which acute pulmonary hypertension affects right ventricular performance are incompletely understood.

Right ventricular vascular load is usually characterized in terms of mean pressure, cardiac output, and pulmonary vascular resistance, all steady-flow measures. However, the hydraulic power cost of generating pulsatile flow is much higher than that computed only from steady-flow terms.[3–5] Therefore, an analysis of pulsatile behavior is necessary to appreciate the impact of pulmonary hypertension on the systolic performance

From the Cardiology Section, Department of Medicine, University of Pennsylvania School of Medicine and the Cardiac Catheterization Laboratory, Hospital of the University of Pennsylvania, Philadelphia, Pa.

Address for correspondence: William G. Kussmaul III, MD, Director, Cardiac Catheterization Laboratory, Pennsylvania Hospital, 301 South 8th Street, Suite 4B, Philadelphia, PA 19106.

Received May 20, 1991; revision accepted August 13, 1992.

of the right ventricle. The vascular impedance spectrum provides a description of the behavior of a system driven by pulsatile flow and includes information concerning proximal vessel stiffness, pulse wave velocity, and arterial wave reflection as well as mean flow, pressure, and resistance. Such data completely define the hydraulic load faced by the ejecting right ventricle.

We report an investigation of steady and pulsatile pulmonary hemodynamics in patients with chronic pulmonary hypertension due to mitral stenosis. The goals of this project were 1) to define the changes in pulmonary artery (PA) impedance and right ventricular-vascular coupling seen in chronic pulmonary hypertension in mitral stenosis, 2) to assess the effects of acute increases in PA pressure by analyzing pulmonary hydraulic properties during pacing tachycardia in these patients, and 3) to determine whether immediate improvement in PA flow dynamics occurred in those patients undergoing catheter balloon valvuloplasty for relief of mitral stenosis.

Methods

Sixteen patients with mitral stenosis form the basis of this report. There were two male and 14 female patients with a mean age of 52 years (range, 20–74 years). Each patient had symptoms and physical findings of rheumatic mitral stenosis, and cardiac catheterization was clinically indicated to define the severity of the disease before consideration of mitral valvuloplasty or valve replacement. In eight patients, the research protocol was carried out at the time of balloon valvuloplasty. Before participation in the study, its nature and risks were explained, and informed consent was obtained in accordance with the policies of the institutional review board.

Catheterization Protocol

All patients were studied in the fasting state after premedication with diazepam or diphenhydramine. A balloon-tipped thermodilution PA catheter was positioned via a femoral vein to record pressures and cardiac output. With a long dilator/sheath set, an 8F high-fidelity catheter also was placed in the PA via a femoral vein. This catheter (Millar Instruments, Inc.) has solid-state pressure transducers located 4, 12, and 20 cm from the tip to allow simultaneous recording of PA, right ventricular, and right atrial pressures. There also was an electromagnetically driven velocity probe mounted at the same site as the distal pressure transducer, energized by a 500-Hz square-wave flowmeter (Carolina Medical Electronics). The sensitivity and frequency response of this system have been reported previously.[6,7] Finally, a 6F pacing catheter was positioned in the right atrium or, for patients with atrial fibrillation, in the right ventricular apex.

Data Recording

All data were recorded with the patients in the supine resting state. For each recording, at least 30 seconds of continuous pressure, velocity, and ECG data were captured on FM magnetic tape, and thermodilution cardiac outputs were obtained in triplicate. The results of those output determinations agreeing within approximately 10% were averaged, and the average was used to scale the velocity signal to volume flow during data analysis. Data were first recorded at the baseline heart rate. In patients with atrial fibrillation ($n=7$), the slowest ventricular pacing rate that overcame atrial competition was taken as baseline. Data were then recorded, including repeat cardiac outputs, after 1 minute at each of several paced rates at increments of 20 min^{-1} until heart rate was 130 beats per minute or a 25% increase in pulmonary wedge pressure was noted. Pacing was discontinued, and the patient was observed during return to the baseline state.

In patients undergoing catheter balloon valvuloplasty, transseptal left atrial puncture was accomplished, and mitral valve dilation was performed using a single large-balloon technique.[8] After ≥15 minutes of stabilization, high-fidelity data and thermodilution cardiac outputs were again recorded at the baseline heart rate and at the highest paced heart rate reached during the prevalvuloplasty protocol.

Data Analysis

The methods for signal-averaging, Fourier analysis of pressure and flow data, and computation of the impedance, power, and reflection spectra have been previously reported.[6,7,9] Pulmonary vascular resistance was computed in standard fashion using cardiac output, mean PA pressure, and mean pulmonary wedge pressure. Impedance moduli were computed from Fourier components of signal-averaged pressure and flow data, averaging at least 25 cycles for each data collection. Characteristic impedance was calculated by averaging the impedance moduli falling between 2 and 12 Hz. This range was selected to avoid the effects of the steep fall in impedance at the first harmonic as well as the possible effects of noise at higher frequencies. In addition, we eliminated pressure and flow harmonics that fell below the Fourier-determined amplitudes of signal-averaged in vitro recordings. These levels were 0.5 mm Hg pressure and 5 ml/sec flow. Because the first harmonic of flow contains a large proportion of the total, the first harmonic of impedance is reported separately.

We resolved the measured pressure and flow waveforms into their forward and reflected components as previously described.[9–11] From the time-domain decomposition into forward and reflected waves, the reflection factor is defined as the ratio of the peak reflected wave amplitude divided by the peak forward amplitude. The timing of the return of the predominant reflected wave to the measuring site in the proximal PA is given both in msec from the onset of ejection and as a fraction of right ventricular ejection time.

Hydraulic power data were derived from Fourier components as follows: Mean dissipated hydraulic power is the product of mean flow (cardiac output) and mean pressure (i.e., pressure gradient across the pulmonary bed). Oscillatory power is that component of external power dedicated solely to producing pulsatile pressure and flow waves. Oscillatory power (W_{osc}) is the sum of power harmonics W_i computed as $W_i=Q_i^2Z_i\cos(\Theta_i)$, where Q_i and Z_i are the flow and impedance moduli, and Θ_i is the impedance phase. Total power (W_T) is the sum of the mean and oscillatory components, and W_{osc}/W_T is the fraction of total dissipated power devoted to producing oscillations. Calculation of hydraulic power alone, however, does not convey the utility of such power output because low flow results in low power expendi-

TABLE 1. Hemodynamic Data

Patient	Age (years)	MV area (cm^2)	Heart rate (bpm)		CO (l/min)		SV (ml)		Mean PAP (mm Hg)		PWP (mm Hg)		RVEDP (mm Hg)	
			Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing
1	32	1.4	75	120	6.2	6.9	82	52	20	25	11	18	6	0
2	35	1.4	80	120	4.0	4.3	59	58	20	25	14	18	7	3
3	43	0.9	72	150	5.1	4.5	66	27	20	25	15	20	4	0
4	43	1.1	62	120	4.4	3.7	72	30	21	30	17	26	5	10
5	65	1.2	87	130	4.8	4.9	54	37	27	35	17	22	8	8
6	20	1.5	64	120	4.2	3.7	61	24	27	40	22	32	10	6
7	68	1.1	79	119	3.7	2.8	46	24	28	37	21	32	8	7
8	63	1.3	71	140	2.8	3.3	39	22	29	35	19	29	8	4
9	56	1.1	89	130	5.3	5.0	61	51	30	39	19	25	2	4
10	61	0.9	77	122	4.7	5.5	60	45	33	46	26	30	10	12
11	63	0.8	103	138	7.1	6.6	68	45	34	37	27	32	8	8
12	58	0.7	78	130	4.2	4.0	53	30	40	43	28	30	9	4
13	56	1.0	90	148	3.2	3.0	35	19	40	51	24	32	14	7
14	74	1.0	98	143	3.4	2.6	34	16	43	50	32	38	10	8
15	50	0.9	91	148	4.6	4.1	50	26	58	61	24	29	8	7
16	43	1.1	84	130	6.4	6.2	72	45	59	63	28	32	7	2
Mean	52	1.0	81	132*	4.6	4.4	57	34*	33	40*	22	28*	8	6†
SD	15	0.2	11	11	1.2	1.3	14	13	12	12	6	6	3	3

MV, mitral valve; CO, cardiac output; SV, stroke volume; PAP, mean pulmonary artery pressure; PWP, mean pulmonary wedge pressure; RVEDP, right ventricular end-diastolic pressure; Pacing, data recorded during pacing tachycardia. Patients are listed in ascending order of mean baseline pulmonary artery pressure.

*$p<0.001$, †$p<0.05$.

ture. Consequently, we also divided total power by the cardiac output to yield W_T/CO, or total hydraulic power expended per unit forward flow. This quantity is a measure of ventricular-vascular coupling because it defines the degree to which expended hydraulic power results in forward flow.

Statistical Analysis

Results are presented as mean±SD. Baseline data were compared with data recorded at the highest paced rate in all 16 patients using a paired *t* test. For the subgroup of eight patients who underwent valvuloplasty, two-way repeated-measures ANOVA was used to determine the effects of pacing and the effects of valvuloplasty. The interaction term was significant for only one variable (pulmonary wedge pressure), where the results of one-way repeated-measures ANOVA were used. Linear regression was used to correlate baseline PA pressures with the values of selected pulmonary vascular properties and to evaluate the relation between patient age and PA properties. In Figure 3, comparisons of harmonics of impedance and flow were done using paired *t* tests with a Bonferroni adjustment. A value of $p<0.05$ was considered significant, although it is recognized that higher *p* values may indicate important trends, especially when the number of observations is small. All statistical computations were carried out using STATVIEW II and SUPERANOVA statistical software (Abacus Concepts, Berkeley, Calif.).

Results

Baseline and Pacing Hemodynamic Data

Cardiac catheterization results in all 16 patients revealed significant mitral stenosis. Table 1 shows baseline hemodynamic data as well as the hemodynamic effects of pacing tachycardia. Mean patient age was 52 years, and the mean calculated mitral valve area was 1.0±0.2 cm^2. As a result of an increase in mean heart rate from a baseline value of 81 to pacing at 132 beats per minute, there were significant reductions in stroke volume and right ventricular end-diastolic pressure. Pulmonary mean pressures increased (pulmonary wedge: 22±6 to 28±6 mm Hg, $p<0.001$; mean PA pressure: 33±12 to 40±12 mm Hg, $p<0.001$). Cardiac output was unchanged (4.6±1.2 to 4.4±1.3 l/min, p=NS). In this and all following tables, patients are presented in ascending order of baseline mean PA pressure.

Baseline and Pacing Impedance and Wave Reflection Data

Baseline PA characteristic impedance averaged 62±25 dyne-sec/cm^5. Table 2 presents the effects of pacing tachycardia on pulmonary resistance, impedance, and reflection properties. During tachycardia, there was no change in pulmonary vascular resistance (209±144 to 232±164 dyne-sec/cm^5, p=NS) or PA characteristic impedance (62±25 to 55±28 dyne-sec/cm^5, p=NS), but impedance at the first harmonic decreased significantly (134±71 to 100±68 dyne-sec/cm^5, $p<0.001$). The frequency at the first impedance minimum tended to increase, although this was not statistically significant. This suggestion of increased pulse wave velocity was strengthened by a significantly earlier arrival time of the reflected pressure and flow waves (307±72 to 270±63 msec). There was no change in the amplitude of these waves when normalized for the amplitude of the incident wave. When reflected wave timing was expressed as a fraction of right ventricular

TABLE 2. Impedance and Wave Reflection Data

	PVR (dyne-sec/cm^5)		Z_1 (dyne-sec/cm^5)		Z_c (dyne-sec/cm^5)		f_{min} (Hz)		RF		BWAT (msec)		BWAT/RVET	
Patient	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing
1	117	91	96	36	65	23	2.5	4.0	0.19	0.36	302	319	0.56	0.76
2	125	125	38	23	14	6	5.4	12.0	0.41	0.47	304	228	0.69	0.60
3	79	88	88	36	78	55	1.2	2.5	0.28	0.28	208	169	0.36	0.37
4	69	89	88	57	47	58	3.1	2.0	0.29	0.46	501	400	1.21	1.31
5	169	214	99	71	54	51	5.8	2.2	0.28	0.28	244	186	0.55	0.44
6	114	150	113	85	44	44	3.2	4.0	0.40	0.57	376	274	0.80	0.76
7	148	125	93	81	47	23	1.3	11.9	0.62	0.74	269	292	0.48	0.71
8	288	152	174	96	79	52	4.7	9.3	0.37	0.30	345	314	0.76	1.14
9	171	224	81	52	22	26	7.4	2.2	0.63	0.52	240	208	0.58	0.55
10	122	230	119	112	93	58	1.3	6.1	0.19	0.54	234	256	0.36	0.56
11	80	62	63	50	77	57	3.4	2.3	0.29	0.38	370	330	1.28	1.28
12	231	259	179	101	97	73	2.6	2.2	0.31	0.13	327	354	0.80	1.13
13	410	510	189	173	80	97	6.0	7.4	0.47	0.36	284	241	0.70	0.70
14	262	374	206	189	96	107	6.5	9.5	0.49	0.38	249	217	0.72	0.74
15	579	619	312	259	60	92	4.5	7.4	0.74	0.77	322	245	0.72	0.72
16	387	399	207	188	42	58	7.0	6.5	0.97	0.72	336	286	0.71	0.76
Mean	209	232	134	100*	62	55	4.1	5.7	0.43	0.45	307	270†	0.70	0.78†
SD	144	164	71	68	25	28	2.1	3.6	0.21	0.18	72	63	0.25	0.28

PVR, pulmonary vascular resistance; Z_1, first harmonic impedance amplitude; Z_c, characteristic input impedance; f_{min}, frequency of first impedance minimum; RF, reflection amplitude ratio; BWAT, backward (reflected) wave arrival time; RVET, right ventricular ejection time; Pacing, data recorded during pacing tachycardia.
*$p<0.001$, †$p<0.05$.

ejection time, the reflection peak occurred later during pacing due to shortened systole at the faster heart rate.

Figure 1 presents the relation of mean PA pressure to selected pulmonary vascular properties in all 16 patients in the resting, baseline state. A strong positive correlation is observed between mean PA pressure and pulmonary vascular resistance ($r=0.84$, $p<0.0001$), first harmonic impedance ($r=0.85$, $p<0.0001$), and the reflection factor ($r=0.72$, $p=0.002$). No such relation can be seen for characteristic impedance.

In Figure 2, the effects of pacing on PA impedance at various rates are shown for one patient. Resistance, first harmonic impedance, and impedance at higher frequencies all decline in this patient. The spectra are similar in overall appearance. Impedance phase first crosses zero at the location of the first modulus minimum. In the group as a whole, however, only first harmonic impedance decreased significantly during pacing tachycardia.

Baseline and Pacing Hydraulic Power Data

Table 3 presents hydraulic power data in the baseline state and during pacing tachycardia. Despite increased mean PA pressure, total dissipated hydraulic power expended per unit forward flow decreased during pacing. Oscillatory power also decreased; therefore, a greater proportion of total power expenditure was directed toward producing forward flow rather than oscillations.

Effects of Valvuloplasty

Tables 4–6 present selected hemodynamic and impedance data in the subset of eight patients who were studied immediately before and after balloon mitral valvuloplasty. Calculated mitral valve areas rose after valvuloplasty from 1.1 to 2.4 cm^2. Baseline heart rate and stroke volume were unchanged (baseline versus valvuloplasty), whereas significant declines in mean PA pressure (37±12 to 27±9 mm Hg) and pulmonary wedge pressure (23±6 to 14±8 mm Hg) were recorded. Pulmonary vascular resistance and characteristic impedance trended downward for the group, but first harmonic impedance decreased significantly (166±75 to 103±45 dyne-sec/cm^5). Oscillatory power decreased when expressed as a fraction of total hydraulic power.

Figure 3 shows the effects of valvuloplasty on resting pulmonary impedance and flow in the eight patients undergoing balloon valvuloplasty. Impedance at low frequencies is significantly diminished after valvuloplasty. It should be noted that this occurs in the same frequency range where flow harmonics have their highest amplitudes.

The effects of pacing tachycardia after valvuloplasty (valvuloplasty versus pacing 2 in Tables 4–6) were similar to those before valvuloplasty except that the increases in wedge and PA pressure were less marked. Total power per unit flow continued to decrease with pacing.

Discussion

The hemodynamic effects of tachycardia in mitral stenosis were delineated more than 20 years ago[1,12,13] in a series of studies showing that decreased diastolic filling time was associated with increased pulmonary pressures. Exercise-induced increases in pulmonary pressures in this condition may also be due to a catecholamine-mediated effect independent of altered heart rate.[13] These effects, coupled with chronically elevated left atrial and pulmonary pressures, eventually lead to compromise of right ventricular performance.[14] However, the corre-

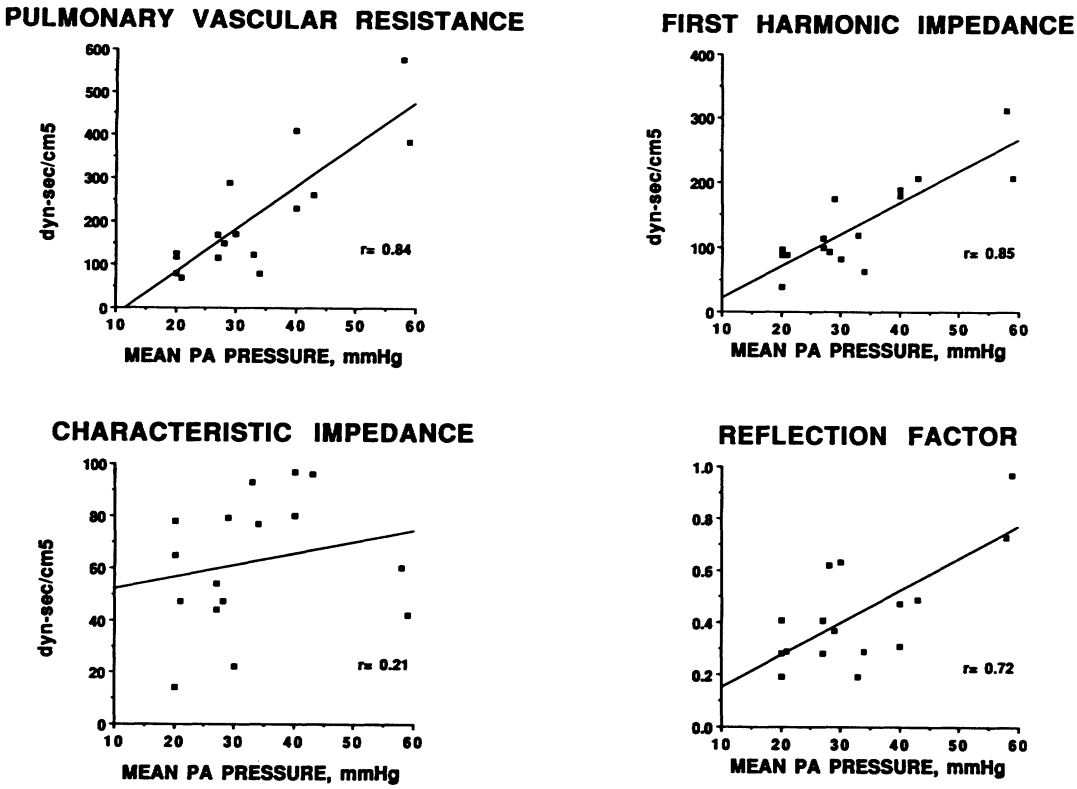

FIGURE 1. *Scatterplots of baseline values of pulmonary vascular resistance, pulmonary artery (PA) impedance at the first harmonic, PA characteristic impedance, and wave reflection factor plotted against mean PA pressure in 16 patients with mitral stenosis in the resting baseline state. Patients with higher mean PA pressure exhibit increased resistance, low-frequency impedance, and reflection amplitudes.*

lation between right ventricular failure and the level of pulmonary hypertension is poor,[15,16] suggesting that factors other than those recognized from nonpulsatile hemodynamic measures may contribute to impaired right ventricular performance in mitral stenosis.

PA Impedance in Chronic Pulmonary Hypertension

Several previous studies have reported alterations in the pulmonary impedance spectrum in chronic pulmonary hypertension.[17–19] The characteristic impedance at the entrance to a vessel is inversely proportional to its cross-sectional area and elasticity. Increased PA characteristic impedance therefore signifies considerable reduction of the distensibility of the major pulmonary arteries[20] since their size is generally increased in pulmonary hypertension compared with normal.[21] The mean characteristic impedance reported here (62±25 dyne-sec/cm^5) is comparable to that previously found in patients with mitral stenosis[17,19] and slightly higher than that found in chronic congestive heart failure.[22] All of these values are elevated in comparison to PA characteristic impedance in normal humans of 20–30 dyne-sec/cm^5.[7,17,19,23] It has previously been assumed that structural changes in the PA wall due to chronic increases in pressure are responsible for altered impedance, as has been found in pediatric patients with pulmonary hypertension due to congenital heart disease.[24] However, the additional effects of acute changes in pulmonary pressure were not examined in any of the previous studies. The absence of change in PA characteristic impedance in the present study during pacing-mediated tachycardia or immediately after balloon mitral valvuloplasty would support the view that structural alteration in arteries resulting from chronic pressure elevation is necessary to produce increased characteristic impedance.

Pulmonary Reflection Characteristics in Mitral Stenosis

Pressure and flow waves in the human pulmonary artery travel at velocities of 2–5 m/sec,[17] making it likely that their return to the arterial inlet occurs during right ventricular ejection. Because pressure reflections are additive to the incident pressure and flow reflections subtract from forward flow,[10] arterial wave reflections have the potential to interfere with optimal ventricular ejection performance. PA wave reflection in patients with mitral stenosis has not been examined previously. In the present study, baseline wave reflection amplitudes averaged 0.43 of the incident wave amplitude, and there was a significant correlation between mean PA pressure and reflected wave amplitude. The peak reflected wave returned, on average, at 70% of the right ventricular ejection time. This suggests that increased PA stiffness, elevated small-vessel resistance, and reflections all contribute to an abnormal right ventricular hydraulic load in mitral stenosis. In the pulmonary circulation, only the studies of Yin and coworkers[25,26] have previously examined wave reflection properties. In their patients with congestive heart failure, PA reflected/forward amplitude ratios ranged from 0.52 to 0.86. These higher values are probably related to greater

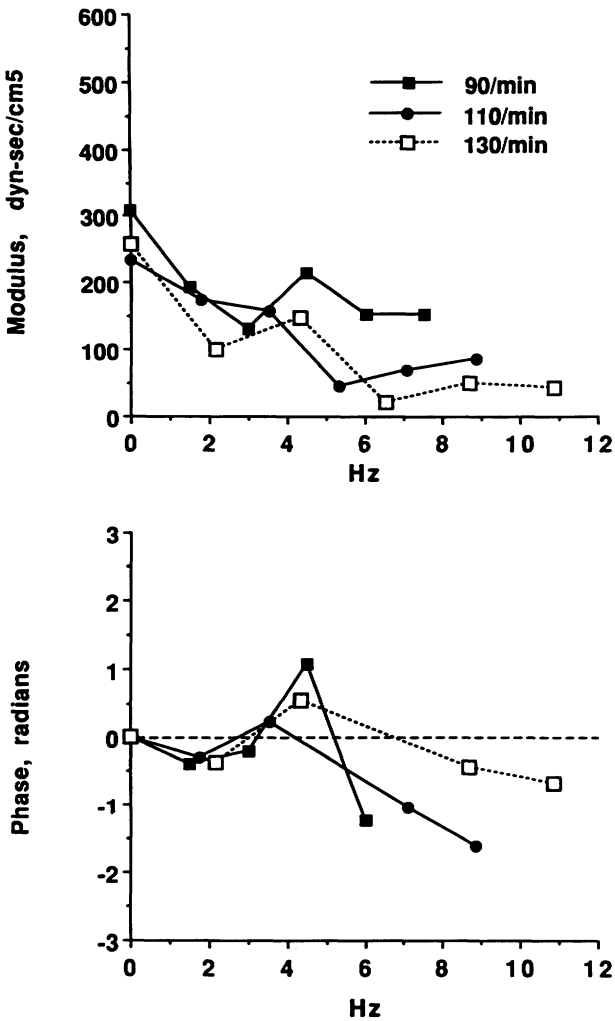

FIGURE 2. *Plots of pulmonary artery impedance spectrum in a single patient at three paced heart rates. Resistance (impedance at 0 Hz) decreases as does the first harmonic modulus. For the group as a whole, only first harmonic impedance decreased significantly during pacing tachycardia.*

degrees of pulmonary hypertension in their patients. In the systemic circulation, wave reflection properties in patients with congestive heart failure have been favorably altered by administration of a vasodilating agent.[9,25,26] The timing and magnitude of the PA reflections reported here imply a significant potential impact on right ventricular ejection performance and suggest that their alteration by pharmacological means would be of therapeutic interest.

Pulmonary Resistance During Acute Pulmonary Hypertension

Few previous reports have considered the effects of acute pulmonary hypertension on pulmonary resistance in humans. In the present study, neither acute pressure increase nor decrease superimposed on chronic pulmonary hypertension altered pulmonary vascular resistance in the group of patients with mitral stenosis as a whole. However, examination of Table 2 reveals that most of the patients with higher baseline resistance or mean PA pressure experienced an increase during pacing, whereas patients at the lower end of the pressure scale experienced a decline or remained unchanged. This finding is consonant with the earlier data of Janicki et al[27] and suggests that patients with less severe chronic pulmonary hypertension retain the ability to recruit additional pulmonary vascular beds during acute increases in pulmonary pressure. This ability may be gradually lost as the chronicity and severity of pulmonary hypertension increase.

Pulmonary Impedance and Wave Reflections During Acute Pulmonary Hypertension

Despite increased mean pulmonary pressure, PA characteristic impedance did not increase during pacing tachycardia. This finding suggests that any reduction in elasticity that occurred due to increased distending pressure was counterbalanced by an increase in PA cross-sectional area. Similar reasoning has been applied to explain a lack of change in aortic impedance during exercise.[28] Constant impedance would tend to preserve ventricular-vascular coupling since optimal coupling is thought to exist at normal levels of pulmonary pressure and impedance.[29,30] The elevated characteristic impedance found in patients with mitral stenosis at baseline appears therefore to be due not merely to the effects of increased pulmonary distending pressure but also to an additional factor such as altered structure of the vascular wall. If this is so, an immediate reduction in impedance would not be expected upon relief of pulmonary hypertension.

Our patients experienced a significant decrease in the amplitude of impedance at the first harmonic during pacing. The reason for this decrease is not entirely clear from our data. Pulmonary impedance spectra typically exhibit a minimum at low frequencies. An increase in the fundamental frequency (i.e., heart rate) would cause the first harmonic to fall further out toward this minimum, resulting in a lower value. This effect can be appreciated from Figure 2, where at each paced rate, impedance modulus values fall from steady state levels toward a minimum at 2–4 Hz.

We did not find any increase in wave reflection amplitude during acute pulmonary hypertension. This may have been related to the lack of change in pulmonary resistance, if pulmonary reflections arise in small pulmonary arteries.[5] The earlier arrival time during pacing is consistent with increased PA stiffness and, therefore, wave propagation velocity. However, any deleterious effect of earlier reflection return was counterbalanced during tachycardia by shorter ventricular ejection time. The net result was that the reflections returned late in systole, when ejection was almost 80% complete. If acute pulmonary hypertension was induced in the absence of increased heart rate, presumably these increased reflections would be more likely to interfere with right ventricular ejection.

Acute Improvement in Pulmonary Dynamics and Impedance After Balloon Mitral Valvuloplasty

Uniform improvement in PA pressures and resistance after relief of mitral stenosis has been previously reported during follow-up after mitral valve replacement.[31] Three previous studies have examined changes in pulmonary resistance after balloon mitral valvuloplasty,[32–34] and all found significant early improve-

TABLE 3. Hydraulic Power Data

Patient	W_{osc} (mW)		W_M (mW)		W_{osc}/W_T		W_T/CO (mW/ml · sec^{-1})	
	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing	Baseline	Pacing
1	81	75	123	108	0.40	0.41	2.0	1.6
2	35	49	54	66	0.40	0.42	1.3	1.6
3	71	5	57	50	0.56	0.09	1.5	0.7
4	53	26	39	33	0.57	0.44	1.2	1.0
5	79	48	106	141	0.43	0.25	2.3	2.3
6	81	21	47	66	0.63	0.24	1.8	1.4
7	35	16	57	31	0.38	0.34	1.5	1.0
8	53	30	62	44	0.46	0.41	2.5	1.3
9	82	77	128	156	0.39	0.33	2.4	2.8
10	69	47	73	195	0.49	0.19	1.8	2.6
11	88	59	110	73	0.44	0.45	1.7	1.2
12	86	46	111	116	0.44	0.28	2.8	2.4
13	66	52	114	126	0.37	0.29	3.4	3.6
14	68	39	82	68	0.45	0.36	2.7	2.5
15	167	75	350	293	0.32	0.20	6.7	5.4
16	178	138	439	424	0.29	0.25	5.8	5.5
Mean	81	50*	122	124	0.44	0.31†	2.6	2.3‡
SD	39	32	112	105	0.09	0.10	1.6	1.4

W_{osc}, oscillatory hydraulic power; W_M, mean dissipated hydraulic power; W_T, total hydraulic power=$W_{osc}+W_M$; W_T/CO, total hydraulic power expended per milliliter of net forward flow; Pacing, data recorded during pacing tachycardia.

*$p<0.001$, †$p<0.05$, ‡$p=0.06$.

ment. The present study did not confirm this finding in the eight patients who underwent balloon dilation, possibly because our patients had less severe pulmonary vascular disease than did those in the earlier series, as indicated by a mean baseline pulmonary vascular resistance of 265 dyne-sec/cm^5 compared with 340 dyne-sec/cm^5 in the series of Block and Palacios,[32] 630 dyne-sec/cm^5 in the report of Levine et al,[33] and 592 dyne-sec/cm^5 in the most recent series of 19 patients reported by Dev and Shrivastava.[34] In the latter report, significant change in resistance did not occur until 1 week after valvuloplasty.

Abnormal low-frequency PA impedance in mitral stenosis, therefore, appears to be in part secondary to labile factors that can be quickly reversed. Reversal of both resistive and high-frequency components may require a longer period of relief from pulmonary hypertension. The present study was not designed to determine the time course of delayed improvements in these parameters, although such data would certainly be of interest.

TABLE 4. Hemodynamics Before and After Valvuloplasty

Patient	Heart rate (bpm)				Stroke volume (ml)				Mean PA pressure (mm Hg)				Pulmonary wedge pressure (mm Hg)			
	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2
1	75	120	84	120	82	52	88	58	20	25	15	17	11	18	6	7
6	64	120	80	120	61	24	57	35	27	40	18	25	22	32	9	15
7	79	119	79	123	46	24	48	17	28	37	26	33	21	32	17	25
10	78	122	82	122	64	45	55	42	37	46	22	26	26	30	10	14
12	90	130	87	130	47	30	76	45	43	43	25	24	26	30	8	11
13	90	148	92	132	35	19	43	28	40	51	37	36	24	32	22	26
14	98	143	97	140	34	16	28	17	43	50	42	44	32	38	30	35
15	91	148	87	142	50	26	65	33	58	61	34	41	24	29	10	15
Mean	83	131*	86	128*	52	30*	58	34*	37	44*	27†	31*†	23	30‡	14§	18§
SD	11	13	6	9	16	13	199	14	12	11	9	9	6	6	8	9

PA, pulmonary artery; PBV, percutaneous balloon valvuloplasty; Baseline, pacing 1, data recorded at rest and during pacing tachycardia just before balloon mitral valvuloplasty; PBV, pacing 2, data recorded at rest and during pacing immediately after valvuloplasty.

*$p<0.01$ pacing vs. baseline.

†$p<0.01$ baseline vs. valvuloplasty.

‡$p<0.05$ pacing vs. baseline.

§$p<0.05$ baseline vs. valvuloplasty.

TABLE 5. Impedance Data Before and After Valvuloplasty

Patient	PVR (dyne-sec/cm^5)				Z_1 (dyne-sec/cm^5)				Z_c (dyne-sec/cm^5)				RF			
	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2
1	117	91	97	113	96	36	42	33	65	23	40	50	0.19	0.36	0.02	0.07
6	114	150	161	180	113	85	72	48	44	44	59	80	0.40	0.57	0.29	0.62
7	148	125	195	250	93	81	68	181	47	23	48	49	0.62	0.74	0.42	0.58
10	169	230	211	188	124	112	97	59	110	58	73	43	0.15	0.54	0.21	0.48
12	318	259	217	179	194	101	102	59	104	73	104	63	0.34	0.13	0.05	0.00
13	410	510	295	206	189	173	119	96	80	97	56	52	0.47	0.36	0.39	0.35
14	262	374	335	293	206	189	183	152	96	107	63	10	0.49	0.38	0.67	0.28
15	579	619	339	412	312	259	144	90	60	92	50	43	0.74	0.77	0.57	0.55
Mean	265	295	231	228	166	130	103*	90*	76	65	62	61	0.42	0.48	0.33*	0.36*
SD	165	191	86	91	75	72	45	52	26	33	20	22	0.20	0.22	0.23	0.25

PVR, pulmonary vascular resistance; Z_1, first harmonic impedance amplitude; Z_c, characteristic input impedance; RF, reflection factor (maximum amplitude of reflected wave/maximum amplitude of forward wave); PBV, percutaneous balloon valvuloplasty; Baseline, pacing 1, data recorded at rest and during pacing tachycardia just before balloon mitral valvuloplasty; PBV, pacing 2, data recorded at rest and during pacing immediately after valvuloplasty.

*$p<0.05$ baseline vs. valvuloplasty.

Importance of Low-Frequency Impedance for Right Ventricular-Vascular Coupling

Our patients experienced no immediate marked improvement in pulmonary characteristic impedance after valvuloplasty, although there was a trend in this direction. A significant fall in first harmonic impedance was recorded, however. Impedance at these low frequencies is particularly important since the first harmonic of flow contains a large proportion of the total flow pulse and more than any other component, including the mean term.[4,23] Therefore, first harmonic impedance should have a significant impact on the hydraulic power requirements placed on the ejecting ventricle. Our data show that a significant fall in hydraulic power requirements did occur, despite unchanged pulmonary resistance. This should allow the ventricle to operate under more favorable circumstances. Figure 3 demonstrates this preponderance of flow information at the first harmonic as well as the significant decrease in impedance at this frequency that follows relief of mitral stenosis. Pulmonary resistance, meanwhile, exhibits a less marked decline. The relative importance of these steady and pulsatile terms has been the subject of numerous laboratory investigations.[35-38] Although changes in mean pressure alone clearly affect ejection performance,[36] pulsatile effects also play an important role.[29,39] In particular, the recent work of Sunagawa and coworkers[38] has shown that pulsatile behavior at low frequencies is quantitatively more important than that at higher frequencies. The present data indicate that reduction in low-frequency impedance is accompanied by increased flow in the same frequency range. This implies improved ventricular-vascular coupling and was demonstrated whenever first harmonic impedance decreased, regardless of whether this occurred during increased or decreased mean PA pressure.

TABLE 6. Power Data Before and After Valvuloplasty

Patient	W_{osc} (mW)				W_M (mW)				W_{osc}/W_T				W_T/CO (mW/ml · sec^{-1})			
	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2	Baseline	Pacing 1	PBV	Pacing 2
1	81	75	92	55	123	108	148	158	0.40	0.41	0.38	0.26	2.0	1.6	1.9	1.8
6	81	21	83	26	47	66	95	94	0.64	0.24	0.47	0.22	1.8	1.4	2.2	1.7
7	35	16	34	9	57	31	77	47	0.38	0.34	0.30	0.16	1.5	1.0	1.7	1.3
10	81	47	57	38	126	195	122	140	0.39	0.19	0.32	0.21	2.4	2.6	2.3	2.0
12	87	46	111	55	162	116	246	169	0.35	0.28	0.31	0.24	3.5	2.4	3.3	2.3
13	66	52	77	62	114	126	136	86	0.37	0.29	0.36	0.42	3.4	3.6	3.1	2.3
14	68	39	45	30	82	68	77	49	0.45	0.36	0.37	0.38	2.7	2.5	2.5	1.9
15	167	75	136	51	350	293	303	291	0.32	0.20	0.31	0.15	6.7	5.4	4.6	4.1
Mean	83	46*	79	41*	132	125	150	129	0.41	0.29†	0.35‡	0.26†‡	3.0	2.6*	2.7	2.2*
SD	38	22	34	18	96	84	82	80	0.10	0.08	0.06	0.10	1.6	1.4	0.9	0.8

W_{osc}, oscillatory hydraulic power; W_M, mean dissipated hydraulic power; W_T, total dissipated hydraulic power; W_T/CO, total dissipated hydraulic power expended per milliliter of net forward flow; PBV, percutaneous balloon valvuloplasty; Baseline, pacing 1, data recorded at rest and during pacing tachycardia just before balloon mitral valvuloplasty; PBV, pacing 2, data recorded at rest and during pacing immediately after valvuloplasty.

*$p<0.01$, †$p<0.05$ pacing vs. baseline.

‡$p<0.05$ baseline vs. valvuloplasty.

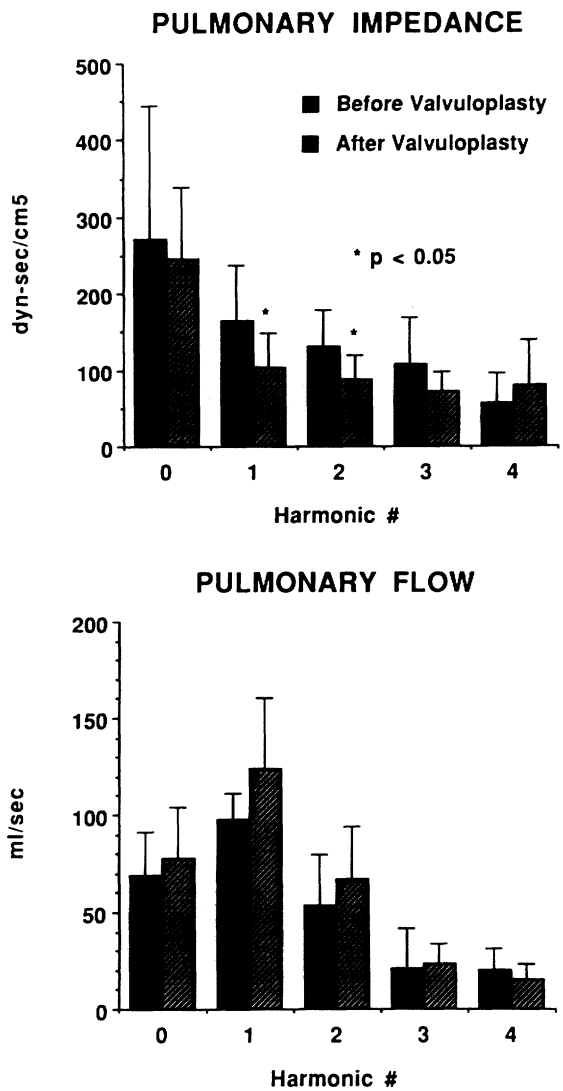

FIGURE 3. *Bar graphs of pulmonary artery impedance and flow moduli for eight patients before and after balloon mitral valvuloplasty. Note the decline in impedance at low frequencies where flow is highest.*

Study Limitations

Application of Fourier analysis and transmission line theory to the vascular system assumes linear behavior of the system. Although this assumption is not entirely justified, the errors introduced by nonlinear behavior have been thoroughly analyzed and appear to be small.[17,40,41] As Figure 2 demonstrates, PA impedance spectra obtained in the same patient at various heart rates are similar in shape.

Single-point determination of flow velocity by a catheter-mounted transducer assumes a relatively blunt velocity profile at the entrance to the great vessel. This assumption has been justified to a limited degree in the animal and human PA.[42,43] The situation is less clear in the presence of pulmonary hypertension. However, velocity signals resembling those reported here have also been found by Doppler methods in patients with pulmonary hypertension,[44] and PA impedance values calculated using an independent velocity method have given results similar to those of the present study in patients with normal and elevated PA pressures.[17] Thus, catheter velocity signals appear to provide a reasonable representation of instantaneous flow velocity in the proximal PA.

The noise inherent in catheter velocity signals is greatly attenuated by time domain signal averaging. This process minimizes any effects of respiration by averaging over at least 25 beats, enough to span several respiratory cycles. In addition, the noise levels of the pressure and flow measuring and recording systems utilized in this study were predetermined, and harmonics of pressure and flow falling below these levels were not included in the analysis. These criteria resulted in exclusion of <10% of harmonics below the seventh.

Mitral valvuloplasty is occasionally complicated by left-to-right shunting through an iatrogenic atrial septal defect. If such shunting occurred in our patients, the calculations of PA resistance and impedance would still be accurate since cardiac output was measured by a PA thermodilution method. Postprocedure systemic and pulmonary oxygen saturations measured after valvuloplasty in four of the eight patients revealed that the pulmonary–to–systemic flow ratio averaged 1.2. It therefore appears unlikely that shunting significantly influenced our results.

Our patient population represents a wide range of ages. There were no significant correlations between the ages of the patients and their baseline hemodynamic characteristics nor with the changes in these quantities during pacing.

Conclusions

The findings of this study may be summarized as follows: 1) chronic pulmonary hypertension in mitral stenosis is associated with elevated pulmonary vascular resistance, impedance, and high-amplitude arterial wave reflections; 2) acute increase in resting pulmonary hypertension does not further elevate characteristic impedance or reflection amplitudes but causes a decrease in low-frequency impedance that is associated with lower pulsatile hydraulic power requirements; 3) amelioration of chronic pulmonary hypertension by relief of mitral stenosis favorably alters PA impedance in that a decrease in low-frequency impedance occurs; and 4) improvement in low-frequency impedance is associated with an increase in flow in the same frequency range and therefore improves right ventricular-vascular coupling. These findings underscore the importance of considering both steady and pulsatile terms when assessing vascular properties. In particular, they direct attention to the pivotal role of low-frequency impedance for determining optimal ventricular hydraulic load. Efforts to treat or prevent right ventricular failure due to pulmonary hypertension might best be directed toward therapies that lower both PA pressure and low-frequency impedance.

Acknowledgments

The staff of the Cardiac Catheterization Laboratory, particularly Carol Davis, RN, and Jane Krol, RN, provided invaluable assistance during the performance of these studies. The authors thank Anna-Marie DiGrazia for help with manuscript preparation.

References

1. Arani DT, Carleton RA: The deleterious role of tachycardia in mitral stenosis. *Circulation* 1967;36:511–516
2. Thompson ME, Shaver JA, Leon DF: Effect of tachycardia on atrial transport in mitral stenosis. *Am Heart J* 1977;94:297–306
3. Caro CG, McDonald DA: The relation of pulsatile pressure and flow in the pulmonary vascular bed. *J Physiol* 1961;157:426–453
4. Milnor WR, Bergel DH, Bargainer JD: Hydraulic power associated with pulmonary blood flow and its relation to heart rate. *Circ Res* 1966;19:467–479
5. O'Rourke MF: Vascular impedance in studies of arterial and cardiac function. *Physiol Rev* 1982;62:570–623
6. Laskey WK, Kussmaul WG, Martin JL, Kleaveland JP, Hirshfeld JW, Shroff S: Characteristics of vascular hydraulic load in patients with heart failure. *Circulation* 1985;72:61–71
7. Kussmaul WG, Wieland JM, Laskey WK: Pressure-flow relations in the pulmonary artery during myocardial ischaemia: Implications for right ventricular function in coronary disease. *Cardiovasc Res* 1988;22:627–638
8. Herrmann HC, Kussmaul WG, Hirshfeld JW: Single large-balloon percutaneous mitral valvuloplasty. *Cathet Cardiovasc Diagn* 1989; 17:59–61
9. Laskey WK, Kussmaul WG: Arterial wave reflection in heart failure. *Circulation* 1987;75:711–722
10. Westerhof N, Sipkema P, Vanden Bos GC, Elzinga G: Forward and backward waves in the arterial system. *Cardiovasc Res* 1972;6: 648–656
11. Li JKJ: Time domain resolution of forward and reflected waves in the aorta. *IEEE Trans Biomed Eng* 1986;33(BME):783–785
12. Kasalicky J, Hurych J, Widimsky J, Dejdar R, Metys R, Stanek V: Left heart haemodynamics at rest and during exercise in patients with mitral stenosis. *Br Heart J* 1968;30:188–195
13. Nakhjavan FK, Katz MR, Maranhao V, Goldberg H: Analysis of influence of catecholamines and tachycardia during supine exercise in patients with mitral stenosis and sinus rhythm. *Br Heart J* 1969; 31:753–761
14. Iskandrian AS, Hakki A-H, Ren J-F, Kotler MN, Mintz GS, Ross J, Kane SA: Correlation among right ventricular preload, afterload and ejection fraction in mitral valve disease. *J Am Coll Cardiol* 1984;3:1403–1411
15. Wroblewski E, James F, Spann JF, Bove AA: Right ventricular performance in mitral stenosis. *Am J Cardiol* 1981;47:51–55
16. Morrison DA, Lancaster L, Henry R, Goldman S: Right ventricular function at rest and during exercise in aortic and mitral valve disease. *J Am Coll Cardiol* 1985;5:21–28
17. Milnor WR, Conti CR, Lewis KB, O'Rourke MF: Pulmonary arterial pulse wave velocity and impedance in man. *Circ Res* 1969; 25:637–648
18. Reuben SR, Kitchin AH: Pulmonary artery input impedance in pulmonary hypertension. *Prog Resp Res* 1975;9:261–266
19. Haneda T, Nakajima T, Shirato K, Onodera S, Takishima T: Effects of oxygen breathing on pulmonary vascular input impedance in patients with pulmonary hypertension. *Chest* 1983;83: 520–526
20. Reuben SR: Compliance of the human pulmonary arterial system in disease. *Circ Res* 1971;29:40–50
21. Greenfield JC, Griggs DM: Relation between pressure and diameter in main pulmonary artery of man. *J Appl Physiol* 1963;18: 557–559
22. Yin FCP, Weisfeldt ML, Milnor WR: Role of aortic input impedance in the decreased cardiovascular response to exercise with aging in dogs. *J Clin Invest* 1981;68:28–38
23. Murgo JP, Westerhof N: Input impedance of the pulmonary arterial system in normal man: Effects of respiration and comparison to systemic impedance. *Circ Res* 1984;54:666–673
24. Lucas CL, Radke NF, Wilcox BR, Henry GW, Keagy BA: Maturation of pulmonary input impedance spectrum in infants and children with ventricular septal defect. *Am J Cardiol* 1986;57: 821–827
25. Yin FCP, Guzman PA, Brin KP, Maughan WL, Brinker JA, Traill TA, Weiss JL, Weisfeldt ML: Effect of nitroprusside on hydraulic vascular loads on the right and left ventricle of patients with heart failure. *Circulation* 1983;67:1330–1338
26. Brin KP, Yin FCP: Effect of nitroprusside on wave reflections in patients with heart failure. *Ann Biomed Eng* 1984;12:135–150
27. Janicki JS, Weber KT, Likoff MJ, Fishman AP: The pressure-flow response of the pulmonary circulation in patients with heart failure and pulmonary vascular disease. *Circulation* 1985;72:1270–1278
28. Murgo JP, Westerhof N, Giolma JP, Altobelli SH: Effects of exercise on aortic input impedance and pressure wave forms in normal humans. *Circ Res* 1981;48:334–343
29. Piene H, Sund T: Flow and power output of right ventricle facing load with variable input impedance. *Am J Physiol* 1979;237: H125–H130
30. Piene H, Sund T: Does normal pulmonary impedance constitute the optimum load for the right ventricle? *Am J Physiol* 1982;242: H154–H160
31. Braunwald E, Braunwald NS, Ross J Jr, Morrow AG: Effects of mitral-valve replacement on the pulmonary vascular dynamics of patients with pulmonary hypertension. *N Engl J Med* 1965;273: 509–514
32. Block PC, Palacios IF: Pulmonary vascular dynamics after percutaneous mitral valvotomy. *J Thorac Cardiovasc Surg* 1988;96:39–43
33. Levine MJ, Weinstein JS, Diver DJ, Berman AD, Wyman RM, Cunningham MJ, Safian RD, Grossman W, McKay RG: Progressive improvement in pulmonary vascular resistance after percutaneous mitral valvuloplasty. *Circulation* 1989;79:1061–1067
34. Dev V, Shrivastava S: Time course of changes in pulmonary vascular resistance and the mechanism of regression of pulmonary arterial hypertension after balloon mitral valvuloplasty. *Am J Cardiol* 1991;67:439–442
35. Wilcken DEL, Charlier AA, Hoffman JIE, Guz A: Effects of alterations in aortic impedance on the performance of the ventricles. *Circ Res* 1964;14:283–293
36. Abel FL, Waldhausen JA: Effects of alterations in pulmonary vascular resistance on right ventricular function. *J Thorac Cardiovasc Surg* 1967;54:886–894
37. Elzinga G, Westerhof N: Pressure and flow generated by the left ventricle against different impedances. *Circ Res* 1973;32:178–186
38. Sunagawa K, Maughan WL, Sagawa K: Stroke volume effect of changing arterial input impedance over selected frequency ranges. *Am J Physiol* 1985;248:H477–H484
39. Pouleur H, Lefevre J, Eyll CV, Jaumin PM, Charlier AA: Significance of pulmonary input impedance in right ventricular performance. *Cardiovasc Res* 1978;12:617–629
40. Reuben SR, Swadling JP, Gersh BJ, Lee GdJ: Impedance and transmission properties of the pulmonary arterial system. *Cardiovasc Res* 1971;5:1–9
41. Milnor WR: *Hemodynamics.* Baltimore, Williams & Wilkins, 1982, p 161
42. Schultz DL, Tunstall-Pedoe DS, Lee GdJ, Gunning AJ, Bellhouse BJ: Velocity distribution and transition in the arterial system, in Wolstenholme GEW, Knight J (eds): *Circulatory and Respiratory Mass Transport.* Boston, Little, Brown & Co, 1969, pp 172–202
43. Reuben SR, Swadling JP, Lee GdJ: Velocity profiles in the main pulmonary artery of dogs and man, measured with a thin-film resistance anemometer. *Circ Res* 1970;27:995–1001
44. Dabestani A, Mahan G, Gardin JM: Evaluation of pulmonary artery pressure and resistance by pulsed Doppler echocardiography. *Am J Cardiol* 1987;59:662–668

Effects of pacing tachycardia and balloon valvuloplasty on pulmonary artery impedance and hydraulic power in mitral stenosis.

W G Kussmaul, 3rd, J A Altschuler, H C Herrmann and W K Laskey

Circulation. 1992;86:1770-1779
doi: 10.1161/01.CIR.86.6.1770
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539