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Research Article

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This study provides no evidence that chronic obstructive pulmonary disease results in chronic impairment of left ventricular function, but on the contrary, has demonstrated that the left ventricle responds normally to an increased pressure load in these patients.

Left Ventricular Function in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT Left ventricular function was assessed in six patients with essentially normal cardiopulmonary function, in five patients with primary myocardial disease, and in 16 patients with chronic obstructive pulmonary disease by determining the response of the ventricle to an increased resistance to ejection. Studies were performed at the time of cardiac catheterization and increased resistance to left ventricular ejection was produced by the intravenous infusion of methoxamine.

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INTRODUCTION

Impairment of cardiopulmonary hemodynamics is a well recognized complication of chronic obstructive pulmonary disease (COPD). Although the manifestations of the hemodynamic abnormalities usually are related to the development of pulmonary hypertension and right ventricular failure, it has been a clinical impression that left ventricular dysfunction also may occur as a complication of the lung disease. Indeed, it is stated in a recent textbook of cardiology that the entire heart is affected in cor pulmonale, and not just the right ventricle (1). Evidence to support this impression has been gained primarily from the observation that patients dying with COPD often have left ventricular hypertrophy at postmortem examination (2–7), and the possible mechanisms for this have been summarized (7). However, the presence of myocardial hypertrophy does not necessarily indicate depressed myocardial function since it has been demonstrated that the hypertrophied myocardium can function normally (8) or even supernormally (9–13). Furthermore, definitive conclusions concerning left ventricular function in these patients cannot be made from the vast amount of hemodynamic data accumulated from cardiac catheterization studied which have been summarized recently (14). None of these studies has been concerned specifically with left ventricular function and the only information pertaining to the function of this ventricle must be inferred from measurements of pulmonary "wedge" pressure at rest and during exercise; this pressure being used as a reflection of left ventricular filling pressure. Interpretation of these "wedge" pressures, however, is extremely difficult since these patients of-

ten have increased intrapleural pressure, particularly during the hyperventilation of exercise, which, in itself, would be expected to elevate intrathoracic vascular pressures.

Recently Ross and Braunwald reported that the response of the left ventricle in man to an increase in resistance to ejection can be used to characterize the functional state of the ventricle (15). Employing this technique, the present study was performed to provide more definitive information concerning left ventricular function in patients with chronic obstructive pulmonary disease.

METHODS

27 patients were the subjects of this study. Six patients, ages 40–52 yr (average, 46) served as controls (Group A). Five of the patients had small mediastinal lesions and this study was performed during diagnostic angiography. The remaining patient in this group had "pure" mitral stenosis with a normal resting pulmonary artery pressure and a calculated mitral valve orifice of 2.5 cm^2. Five patients, ages 41–55 yr (average, 46), had primary myocardial disease (Group B). Each of these patients had cardiomegaly, whereas three of the five had a history of congestive heart failure and were receiving a digitalis preparation. None of these patients had congestive heart failure clinically at the time of the study. 16 patients, ranging in age from 41 to 76 yr (average, 54), had clinical and radiographic evidence of obstructive pulmonary disease (Group C). None of these patients had systemic hypertension, evidence of valvular disease, previous myocardial infarction, or a history of angina pectoris.

Pulmonary function tests were performed in each of the patients with COPD within 72 hr of cardiac catheterization. Spirometric measurements of the divisions of lung volume and maximum breathing capacity were determined in each subject whereas functional residual capacity was measured by the closed circuit nitrogen washout technique in 14 of the 16 patients. Alveolar nitrogen was measured after breathing 100% O_2 for 7 min. In addition, the diffusing capacity of carbon monoxide was measured by the single breath method in 10 of the patients. Arterial O_2 saturation was determined spectrophotometrically and arterial pCO_2 and pH with a direct-reading electrode instrument (IL meter, Instrumentation Laboratory, Boston, Mass.) Pulmonary function tests were not performed in the control patients or in those with primary myocardial disease, however none had clinical or radiographic evidence of pulmonary disease.

After right heart catheterization, a catheter was inserted retrogradely into the left ventricle in each patient for the measurement of pressure. Brachial arterial pressure and a standard limb lead of the electrocardiogram were recorded in each patient. Cardiac output was determined by the indicator-dilution method with injection of indocyanine green dye into the pulmonary artery and sampling from the brachial artery. Left ventricular ejection time was determined from an indirect carotid arterial pulse tracing recorded at a paper speed of 100 mm/sec. All pressures were measured with Statham P23Gb transducers (Statham Instruments, Inc., Los Angeles, Calif.) with the mid-thoracic level used as the zero reference point. Pressures were averaged over three complete rspiratory cycles. All measurements were recorded on a multichannel oscillograph.

After control observations, methoxamine, a sympathomimetic amine without significant beta adrenergic effect (16), was infused intravenously at a rate necessary to produce a 40–50% increase in systole arterial pressure. All measurements were then repeated when systemic arterial pressure, heart rate, and LVEDP had remained constant for 3–5 min. Left ventricular stroke work index (SWI) in g-m/m^2 was calculated from the following formula:

$$SWI = \frac{SVI \times (LVS - LVEDP) \times 1.36}{100},$$

where SVI equals the stroke volume index in milliliters per square meter; LVS equals the mean left ventricular pressure during ejection in mm Hg determined by planimetric integration; and LVEDP equals left ventricular end-diastolic pressure in mm Hg. Because it has been reported that changes in myocardial function can occur which may not affect SVI or SWI, but which will produce alterations in parameters dependent on the rate of ventricular contraction (17), stroke power index (SPI) in g-m/sec per m^2 was determined by dividing SWI by the ejection period in seconds.

RESULTS

The results of the pulmonary function tests in the patients with COPD are given in Table I. 15 patients had a reduced vital capacity, while all 16 patients had a reduced 1-sec vital capacity and maximum voluntary ventilation. In addition, the ratio of residual volume to total lung capacity was increased in each of 14 patients in whom it was determined. Furthermore, an increased total lung capacity, evidence of impaired distribution of inspired air, and a reduced diffusing capacity of carbon monoxide commonly were observed. Oxygen saturation at rest ranged from 60–95% and was less than 90% in 9 of the 16 patients. Arterial pH was within the normal range in each patient at the time of the study, while arterial pCO_2 exceeded 45 mm Hg in only four patients (E. Z., J. C., P. S., and H. L.). Although this group consisted of both those patients with predominant chronic bronchitis and those with predominant pulmonary emphysema, their responses to methoxamine were similar; therefore, they have been grouped together.

TABLE I

Results of the Pulmonary Function Tests in Group C Patients

Patient	VC		FEV 1.0/ VC	MVV		Alv N_2	RV		TLC		RV/ TLC	DLCO	Art O_2 sat
	ml	*% predicted*	*%*	*liters/min*	*% predicted*	*%*	*ml*	*% predicted*	*ml*	*% predicted*	*%*	*ml/min per mm Hg*	*%*
1 R. Wal.	2100	(61)	48	35	(38)	3.0	3972	(227)	6072	(121)	65	19.3	93
2 R. Wag.	2000	(54)	70	39	(42)	—	—		—		—	37.8	92
3 R. H.	4825	(111)	38	83	(63)	2.8	3690	(186)	8515	(151)	43	42.0	94
4 L. T.	2400	(63)	48	33	(33)	—	—		—		—	21.0	93
5 K. H.	2825	(77)	46	43	(42)	2.0	2005	(108)	4830	(91)	42	—	92
6 E. Z.	2225	(57)	26	34	(34)	—	4125	(209)	6350	(113)	65	18.7	76
7 L. W.	1200	(29)	42	14	(12)	3.1	4616	(250)	5816	(109)	79	—	82
8 W. H.	1830	(51)	39	31	(34)	2.9	2925	(160)	4755	(91)	62	—	86
9 G. W.	2100	(56)	14	25	(24)	2.3	3152	(192)	5252	(112)	60	23.1	86
10 J. G.	1050	(29)	57	28	(30)	—	4307	(240)	5357	(103)	80	—	92
11 P. S.	1650	(41)	48	24	(19)	2.8	5049	(246)	6699	(114)	75	—	80
12 T. J.	1550	(48)	39	14	(19)	3.2	2204	(134)	3754	(80)	59	15.6	95
13 B. L.	2450	(72)	40	49	(76)	—	4959	(288)	7409	(151)	67	5.0	86
14 M. W.	1000	(28)	12	23	(25)	2.4	5406	(301)	6466	(124)	85	12.1	85
15 J. C.	1400	(36)	30	36	(36)	2.6	2409	(136)	3809	(75)	63	20.4	80
16 H. L.	1850	(47)	57	25	(23)	4.4	3223	(178)	5073	(98)	64	—	60

VC, vital capacity; FEV 1.0/VC, timed vital capacity; MVV, maximum voluntary ventilation; Alv N_2, alveolar nitrogen; RV, residual volume; TLC, total lung capacity; DLCO, diffusing capacity for carbon monoxide; Art O_2 sat, arterial oxygen saturation.

TABLE II

Effects of Methoxamine on Patients in Group A

Patient BSA		Heart rate	Art. press. S/D	Art. press. Mean	CI	LVEDP	SVI	SWI	SPI	Mean PA press.
			mm Hg		*liters/min per m²*	*mm Hg*	*ml/m²*	*g-m/m²*	*g-m/sec per m²*	*mm Hg*
N. S.	C	88	147/82	104	4.39	4	50	79	346	18
1.57	M	60	187/92	124	3.57	5	60	118	378	—
J. B.	C	100	85/55	69	2.46	1	25	24	110	—
1.71	M	80	123/74	92	2.35	0	29	38	177	—
E. R.	C	78	131/81	98	3.41	8	44	61	202	18
1.84	M	66	184/102	129	2.89	14	44	78	236	—
H. C.	C	70	125/70	88	2.51	9	36	43	155	17
1.88	M	50	171/80	110	2.05	13	41	69	197	—
G. B.	C	76	172/87	115	3.49	7	46	87	310	19
1.82	M	52	214/93	133	2.90	18	56	121	379	—
R. B.	C	84	130/72	91	5.13	3	61	97	374	19
1.75	M	60	205/88	127	4.56	12	76	162	451	—
Mean	C	83	131/75	94	3.57	5	44	65	250	
± SEM	M	±4.3		±6.4	±0.43	±1.3	±5.0	±16.4	±44.4	
	M	61*	181/88*	119*	3.05*	10*	51*	98*	303*	
		±4.4		±6.3	±0.37	±2.7	±6.7	±18.1	±46.5	

BSA, body surface area in m²; Art. press., systemic arterial pressure, S/D, systolic diastolic; CI, cardiac index; LVEDP, left ventricular end-diastolic pressure; SVI, stroke volume index; SWI, stroke work index; SPI, stroke power index; PA press., pulmonary artery pressure. C, control; M, during methoxamine infusion.

* Mean significantly different from control ($P < 0.05$).

The hemodynamic data for each individual before and during methoxamine infusion are presented in Tables II, III, and IV.

Group A (Table II)

Mean systemic arterial pressure increased in each patient from an average of 94 mm Hg at rest to 119 mm Hg during methoxamine infusion. Heart rate, which averaged 83 beats/min during the control period, decreased in each patient to an average of 61 beats/min. Cardiac index (CI) decreased from an average of 3.57 liters/min per m^2 at rest to 3.05 liters/min per m^2 during drug infusion, decreasing in five or six patients. Resting LVEDP averaged 5 mm Hg and increased to 10 mm Hg, rising in five patients. During the administration of methoxamine, SVI increased in five patients, whereas SWI and SPI increased in all six. SVI averaged 44 ml/m^2 at rest and 51 ml/m^2 during drug infusion, whereas SWI increased from an average of 65 to 98 g-m/m^2, and SPI from a mean of 250 to 303 g-m/sec per m^2.

Group B (Table III)

Mean systemic arterial pressure averaged 88 mm Hg at rest and increased in each patient to an average of 107 mm Hg with methoxamine. Heart rate decreased from an average of 88 to 81 beats/min, decreasing in each patient. Cardiac index at rest was reduced (< 2.5 liters/min per m^2) in only one patient and averaged 3.18 liters/min per m^2. During methoxamine infusion, CI decreased in each patient to an average of 2.33 liters/min per m^2. LVEDP at rest averaged 11 mm Hg and exceeded 12 mm Hg in only two patients. With methoxamine LVEDP rose to abnormal levels in every patient and averaged 21 mm Hg. Concomitantly SVI decreased in all five patients, whereas both SWI and SPI fell in four patients and were unchanged in the remaining one. SVI decreased from a resting average of 37 to 29 ml/m^2, SWI from 44 to 39 g-m/m^2, and SPI from 180 to 146 g-m/sec per m^2.

Group C (Table IV)

Mean systemic arterial pressure averaged 88 mm Hg at rest and increased in each patient with methoxamine to an average of 116 mm Hg. Heart rate decreased from a mean of 91 to 80 beats/min, decreasing in 14 patients. CI was less than 2.50 liters/min per m^2 at rest in four patients and averaged 2.58 liters/min per m^2. However, CI did

TABLE III

Effects of Methoxamine on Patients in Group B

Patient BSA		Heart rate	Art. press. S/D	Art. press. Mean	CI	LVEDP	SVI	SWI	SPI	Mean PA press.
			mm Hg		*liters/min per m^2*	*mm Hg*	*ml/m^2*	*g-m/m^2*	*g-m/sec per m^2*	*mm Hg*
R. V.	C	80	118/68	84	3.03	6	38	45	182	24
1.67	M	77	157/78	109	2.20	22	29	41	133	—
R. Si.	C	95	136/88	102	3.70	3	39	54	256	18
1.92	M	90	157/92	116	2.70	16	30	44	196	—
R. Sa.	C	80	123/77	94	4.00	23	50	61	216	35
2.00	M	74	143/92	112	3.50	28	47	61	216	—
F. S.	C	88	96/61	72	2.76	18	31	29	119	29
1.91	M	82	105/74	84	1.87	22	23	23	104	—
C. S.	C	95	112/67	87	2.40	4	25	31	128	14
2.00	M	82	155/91	114	1.40	16	17	24	81	—
Mean	C	87	117/72	88	3.18	11	37	44	180	
± SEM		±3.4		±5.0	±0.30	±4.1	±4.2	±6.3	±26.0	
	M	81*	143/85*	107*	2.33*	21*	29*	39*	146*	
		±2.7		±5.9	±0.36	±2.2	±5.0	±7.0	±26.0	

See Table II for abbreviations.

TABLE IV

Effects of Methoxamine on Patients in Group C

Patient BSA		Heart rate	Art. press. S/D	Art. press. Mean	CI	LVEDP	SVI	SWI	SPI	Mean PA Press.
			mm Hg		*liters/min per m²*	*mm Hg*	*ml/m²*	*g-m/m²*	*g-m/sec per m²*	*mm Hg*
1 R. Wal.	C	70	124/64	84	3.05	0	44	58	182	14
1.77	M	72	172/84	113	3.61	3	50	86	240	—
2 R. Wag.	C	85	108/68	81	2.70	6	32	39	163	15
1.52	M	56	138/78	98	2.57	11	46	66	205	—
3 R. H.	C	68	122/72	89	3.42	5	50	66	219	16
2.04	M	66	196/98	131	3.30	11	50	106	379	—
4 L. T.	C	88	120/68	85	2.57	4	29	39	134	20
1.64	M	74	160/106	124	2.64	8	36	57	196	—
5 K. H.	C	88	170/93	119	2.84	5	32	59	236	16
1.75	M	80	203/97	132	3.29	10	41	90	300	—
6 E. Z.	C	81	120/75	90	3.16	10	39	54	216	35
1.67	M	62	180/95	123	2.81	13	45	81	272	—
7 L. W.	C	100	125/85	98	2.94	10	29	45	187	36
1.78	M	100	170/104	126	3.23	17	32	56	233	—
8 W. H.	C	90	131/78	96	2.82	6	31	44	162	24
1.59	M	72	194/100	133	2.77	28	38	76	230	—
9 G. W.	C	104	100/60	73	2.90	5	28	33	145	31
1.72	M	92	160/90	113	2.86	6	31	53	222	—
10 J. G.	C	96	166/76	106	1.90	5	20	37	132	26
1.80	M	72	216/83	127	2.36	7	33	68	261	—
11 P. S.	C	84	90/56	70	2.62	6	31	31	141	—
2.12	M	74	137/88	102	3.43	8	46	69	278	—
12 T. J.	C	100	100/70	80	1.94	12	19	21	94	30
1.52	M	96	150/80	103	1.96	16	20	31	114	—
13 B. L.	C	102	116/78	83	1.14	5	11	13	94	30
1.60	M	94	160/92	114	1.41	5	15	26	175	—
14 M. W.	C	88	120/73	93	2.63	12	30	38	167	30
1.53	M	78	160/88	118	2.81	17	36	60	187	—
15 J. C.	C	84	105/65	78	1.70	6	20	23	113	58
1.60	M	78	160/86	111	1.90	14	24	40	166	—
16 H. L.	C	126	119/67	84	3.01	7	24	32	152	35
1.78	M	108	126/71	89	2.85	2	26	38	171	—
Mean	C	91	121/72	88	2.58	7	29	40	159	
± SEM		±3.5		±3.1	±0.15	±0.8	±2.4	±3.6	±10.5	
	M	80*	168/90*	116*	2.74	11*	36*	63*	227*	
		±3.6		±3.3	±0.15	±1.6	±2.7	±5.6	±15.8	

See Table II for abbreviations.

not fall significantly in any patient during drug infusion and averaged 2.74 liters/min per m². LVEDP did not exceed the upper limits of normal in any patient at rest and averaged 7 mm Hg. With methoxamine, LVEDP increased in 14 of the 16 patients but only to an average of 11 mm

Hg. In response to the increased afterload, SWI and SPI increased in each patient whereas SVI increased in 15 subjects and was unchanged in the other. SVI increased from an average of 29 ml/m² at rest to 36 ml/m², SWI from 40 to 63 g-m/m², and SPI from 159 to 227 g-m/sec per m².

Because it seemed possible that impairment of left ventricular function in patients with COPD might occur only in those with the more advanced pulmonary disease, these patients were divided into three groups and the results were compared. Furthermore, since this study was concerned with cardiac function, it appeared more advisable to base this division on the level of pulmonary artery pressure and the occurrence of right ventricular failure, rather than the severity of impairment of pulmonary function. One group (C1) consisted of five patients with a resting mean pulmonary artery pressure of 20 mm Hg or less. The second group (C2) was composed of five patients with a mean pulmonary artery pressure at rest of greater than 20 mm Hg, but who had never manifest right ventricular failure. The remaining group (C3) consisted of six patients with resting pulmonary hypertension and a history of right ventricular failure. The individual hemodynamic data before and during drug administration are presented in Table IV where Group C1 consists of patients 1–5; C2, 6–10; and C3, 11–16. The mean values of the various parameters for these three groups are illustrated in Figs. 1 and 2.

Group C1

Mean systemic arterial pressure averaged 92 mm Hg during the control period and increased to 120 mm Hg during methoxamine infusion. Heart rate decreased from a resting average of 80 to 70 beats/min. CI was within normal limits at rest in

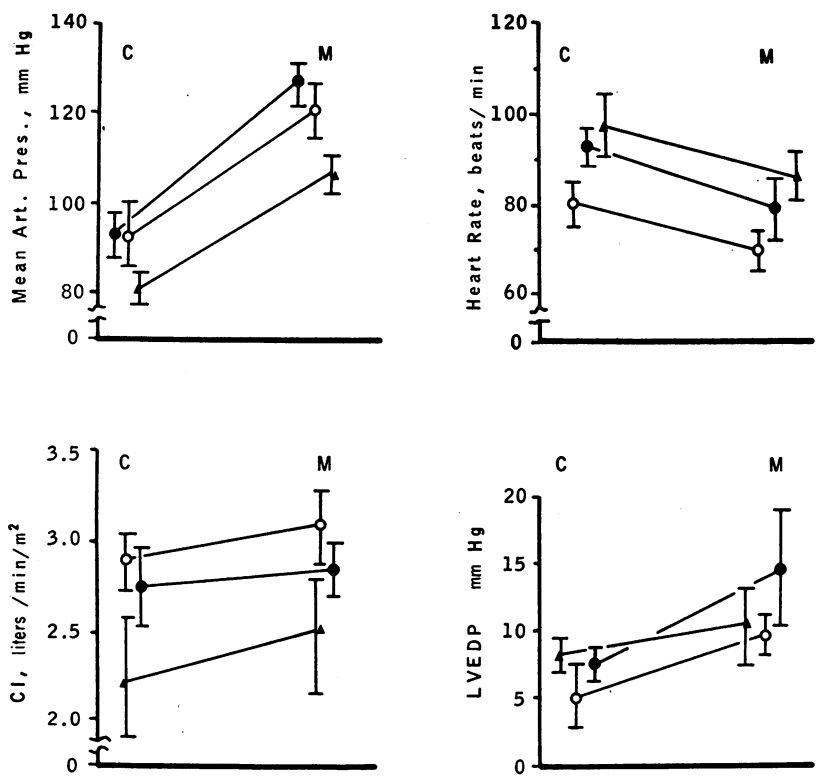

FIGURE 1 Hemodynamic changes during the infusion of methoxamine in patients with chronic obstructive pulmonary disease. Open circles represent patients with normal resting pulmonary artery pressure; closed circles, those with resting pulmonary hypertension; and closed triangles, those who had demonstrated right ventricular failure. Points represent mean values ± SEM. CI, cardiac index; Mean Art. Pres., mean systemic arterial pressure; LVEDP, left ventricular end-diastolic pressure; *C*, control period; *M*, during methoxamine infusion.

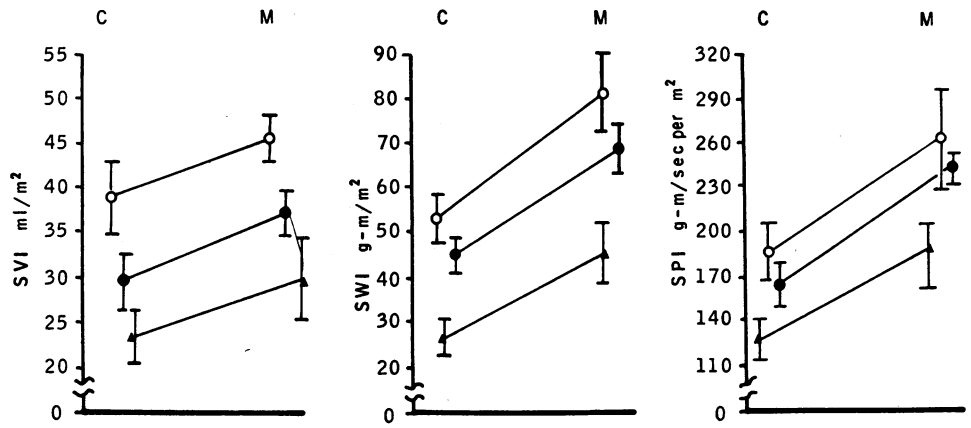

FIGURE 2 The effect of methoxamine on stroke volume index (SVI), stroke work index (SWI), and stroke power index (SPI) in patients with chronic obstructive pulmonary disease. For symbols see Fig. 1.

each patient, averaging 2.92 liters/min per m², whereas with methoxamine CI averaged 3.08 liters/min per m². LVEDP averaged 4 mm Hg at rest and increased to an average of 9 mm Hg. With increased afterload, SVI increased from a resting average of 37 to 45 ml/m², SWI from 52 to 81 g-m/m², and SPI from 187 to 264 g-m/sec per m². Resting mean pulmonary artery pressure averaged 16 mm Hg and arterial oxygen saturation 93%.

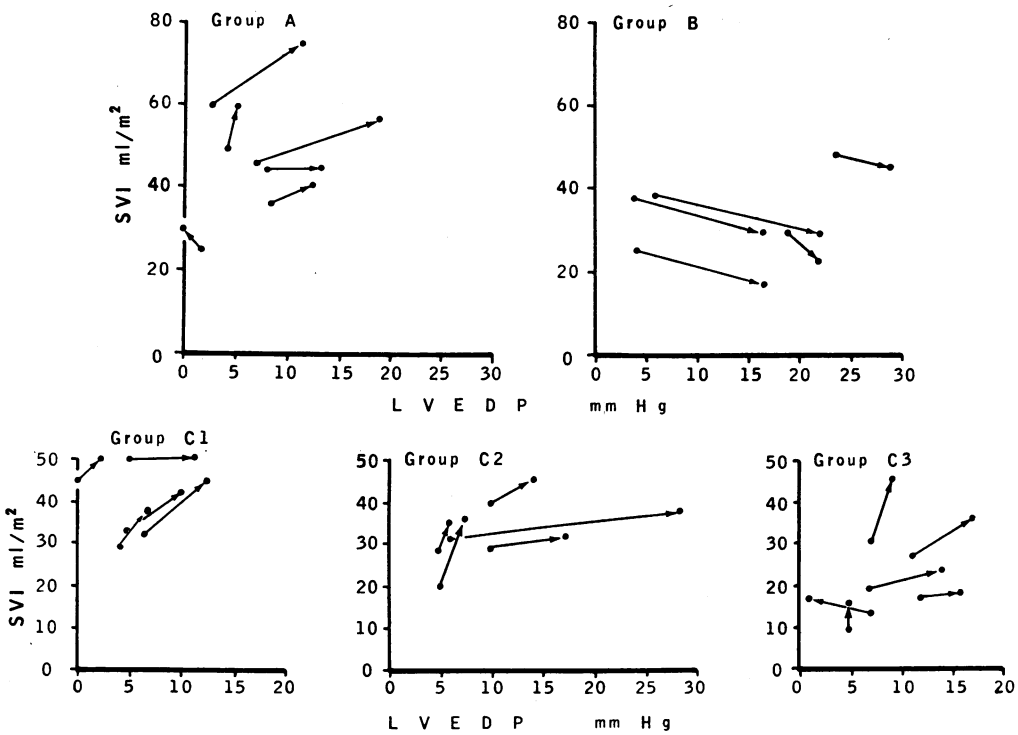

FIGURE 3 The effect of methoxamine on the relationship of stroke volume index (SVI) to left ventricular end-diastolic pressure (LVEDP) in each individual patient. Arrows point to values during methoxamine infusion. For classification of group see text.

Group C2

Mean systemic arterial pressure averaged 93 mm Hg and increased to 124 mm Hg with methoxamine. Heart rate decreased from an average of 94 to 80 beats/min. CI at rest was less than 2.50 liters/min per m^2 in only one patient and averaged 2.74 liters/min per m^2. During methoxamine infusion, CI averaged 2.81 liters/min per m^2. LVEDP averaged 7 mm Hg during the control period and 14 mm Hg during drug administration. One patient, W. H., did demonstrate an inordinate increase in LVEDP, from 6 to 28 mm Hg. With methoxamine, SVI rose from an average of 29 to 36 ml/m^2, SWI from 43 to 67 g-m/m^2, and SPI from 168 to 244 g-m/sec per m^2. Mean pulmonary artery pressure at rest averaged 30 mm Hg and arterial oxygen saturation 86%.

Group C3

Mean systemic arterial pressure averaged 81 mm Hg and increased to an average of 106 mm Hg during methoxamine, whereas heart rate decreased from a control average of 97 to 88 beats/min. Resting CI was less than 2.50 liters/min per m^2 in three of the six patients and averaged 2.17 liters/min per m^2. With methoxamine CI averaged 2.39 liters/min per m^2. LVEDP averaged 8 mm Hg at rest and 10 mm Hg during the increase in resistance to ejection. This was accompanied by an increase in SVI from an average of 23 to 28 ml/m^2, in SWI from 26 to 44 g-m/m^2, and in SPI from 127 to 182 g-m/sec per m^2. Mean pulmonary artery pressure at rest averaged 37 mm Hg in the five patients in whom it was determined. Right ventricular systolic pressure was 41 mm Hg in the remaining patient. Arterial O_2 saturation averaged 81%.

For comparative purposes, the relationship of SVI and SWI to LVEDP, i.e. ventricular function "curves," for each subject in all groups are illustrated in Figs. 3 and 4. Since the relationship of SPI to LVEDP was essentially identical to that of SWI and LVEDP in each patient, these are not presented. In the control patients, an increase in LVEDP was associated with an increase in SWI in each patient and an increase in SVI

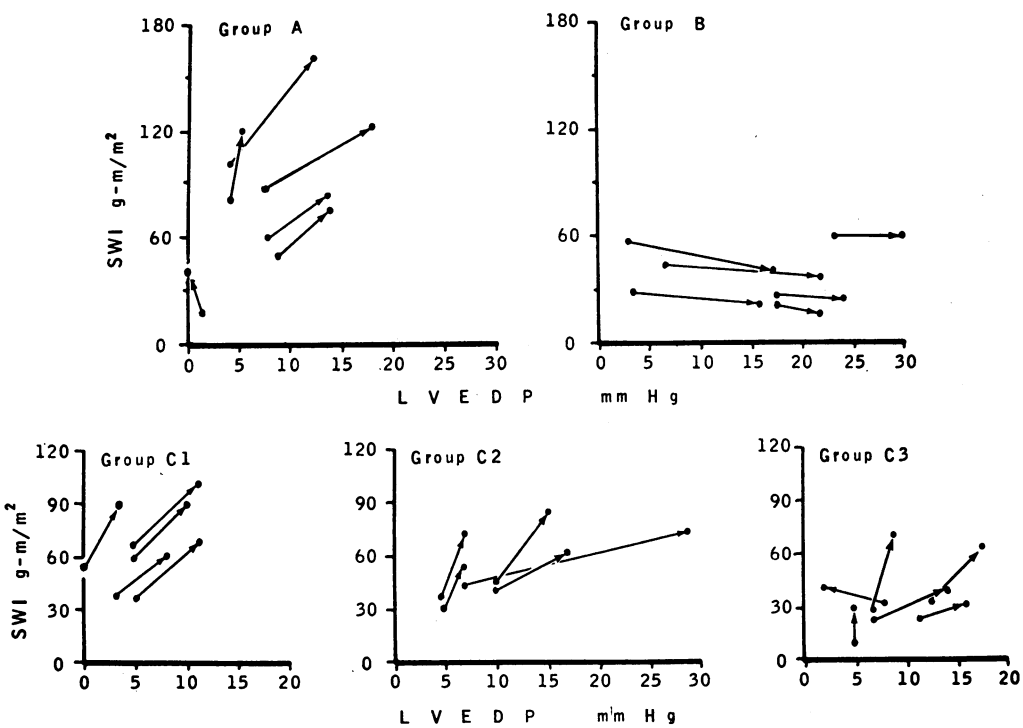

FIGURE 4 The effect of methoxamine on the relationship of stroke work index (SWI) to left ventricular end-diastolic pressure (LVEDP) in each individual patient. Arrows point to values during methoxamine infusion. For classification of group see text.

in five of the six subjects. In contrast, in patients with myocardiopathy, although LVEDP generally increased to an even greater extent, SVI fell in each patient and SWI decreased in four of the five. With one exception, these relationships in all patients with COPD were quite similar to those of the control patients, comparable increases in LVEDP being associated with increases in SWI in each patient and SVI in 15 of the 16 patients.

DISCUSSION

Recently Ross and Braunwald demonstrated that it was possible to characterize the functional state of the left ventricle in man by determining its response to an increased afterload produced by the infusion of angiotensin (15). They observed that the normal ventricle responded to an increased resistance to ejection with an increase in SWI and SVI, whereas LVEDP increased only moderately. In contrast, although LVEDP increased to an even greater extent, SWI and SVI fell in those patients with abnormal left ventricular function. These observations were supported by previous experiments using isolated hearts (18), intact hearts (19), and isolated muscle preparations (19, 20).

The results of the present study in which methoxamine was employed to increase afterload in patients with essentially normal cardiac function (Group A) and those with myocardiopathy (Group B), therefore, are in agreement with the results obtained by Ross and Braunwald. It is of interest that such distinctly abnormal responses were observed in each of the patients with myocardiopathy, even though left ventricular function often appeared normal at rest, i.e., CI was normal in four and LVEDP in three of these patients. The infusion of methoxamine into patients with COPD revealed that the left ventricular response in these patients was similar to that of the control patients with no statistically significant differences existing between these two groups in the response of LVEDP, SVI, SWI, or SPI. In contrast, highly significant differences exist between the patients with COPD and those with myocardiopathy in the response of each of these variables.

However, it must be appreciated that the decrease in heart rate during methoxamine infusion was significantly greater in the control patients than in those with COPD. Since differences in the response of heart rate might well produce differences in the response of SVI, and consequently SWI and SPI, comparison of these responses in these two groups must be made with caution. The necessity for making a truly quantitative comparison between these two groups is evident from the observations of Ross and Braunwald. They observed patients, classified as having depressed myocardial function, in whom SVI and SWI increased with increased pressure load but not to an appropriate degree when compared to the increase in LVEDP (15). Therefore although the patients with COPD clearly do not have left ventricular dysfunction of the severity manifest by Group B, it could not be established conclusively that left ventricular function is normal in the pulmonary disease patients by comparing their response solely with that of the controls. However, when the patients with lung disease were divided into groups on the basis of their impairment of cardiopulmonary hemodynamics at rest and the results compared, strong evidence is provided that left ventricular function is well maintained in this disease.

Regardless of whether these patients with COPD had essentially normal resting hemodynamics or whether they had progressed to the stage of right ventricular failure, essentially identical responses to methoxamine were observed. During the infusion of methoxamine, similar increases in systemic arterial pressure and decreases in heart rate occurred in these three groups of patients (C1, C2, and C3). SVI, SWI, and SPI rose, whereas LVEDP increased moderately in each group with no statistically significant differences observed between these groups in the response of any of these variables. Further statistical analyses comparing the response with methoxamine of each of the group of patients with COPD with that of the control patients revealed that the decrease in heart rate in Group C3 was the only one of the above variables significantly different statistically from those of the Group A patients. In contrast, even in the patients with COPD who had manifest right ventricular failure (Group C3), highly significant differences in the response of SVI, SWI, SPI, and LVEDP and insignificant differences in the changes in heart rate and systemic arterial pressure were observed when compared with those of the patients with myocardiopathy.

It is apparent that the resting cardiac index of the patients with COPD was less than that of the control patients and that this variable decreased progressively as the severity of pulmonary hemodynamics increased. In view of the results of this study, this most likely represents the effect of chronic pulmonary hypertension on right ventricular function. If this were due to left ventricular dysfunction, it would not be expected that SVI, SWI, and SPI would increase with increased afterload, since impairment of left ventricular function, which is not even of the severity to reduce resting CI or elevate LVEDP, still produces such distinctly abnormal responses to increased resistance to ejection (Group B). The effect that the decrease in CI and consequent decrease in SVI might have on the left ventricular response to increased resistance to ejection can be ascertained from previous studies in animals. In experiments in which stroke volume was controlled, it was demonstrated that as the resting stroke volume was increased in the normal ventricle, greater increases in stroke work were produced by similar increases in resistance to ejection (18, 19). Therefore, the observation that the response of SWI and SPI was no less in Groups C2 and C3, with their lower resting stroke volumes, than in the controls or Group C1 even though a somewhat diminished response might have been expected only strengthens the conclusion that left ventricular function was normal in these patients.

The observation that the resting LVEDP was higher and the resting CI lower in Groups C2 and C3 than the control patients or those in Group C1 might be used as evidence that myocardial function was depressed in the former two groups. However conclusions based on single measurements of LVEDP in patients with obstructive lung disease are potentially erroneous since these values probably do not reflect the true end-diastolic pressure in this chamber. The use of the same fixed point on the thoracic cage as the reference point for zero pressure in patients with normal thoracic cages and in those with increased anteroposterior diameter could lead to apparent differences in intravascular pressure if the geometric relationship of the left ventricular cavity to the reference point were different. Also, it is well known that intrathoracic pressure may be elevated in patients with COPD. This in itself could result in an apparent elevation of LVEDP, although transmural pressure might be normal. Regardless of whether the LVEDP as measured in the patients with COPD represents the true LVEDP, the determination of changes in LVEDP in these patients should be accurate in the absence of changes in ventilation or airway resistance. Respiratory rate was not affected significantly by methoxamine infusion in any of the patients in the present study. Furthermore, minute ventilation was determined in three patients with lung disease and intra-esophageal pressure in three other patients with COPD and no changes were observed during drug administration.

The usefulness of employing changes in LVEDP to assess left ventricular function as performed in this study is dependent upon the ability of this variable to reflect changes in end-diastolic ventricular volume. Although direct measurement of end-diastolic volume would be preferable when possible, considerable evidence has been presented that changes in LVEDP do reflect changes in end-diastolic fiber length (17, 21, 22).

One patient in Group C2 (W. H.) responded in a manner similar to that of patients with depressed myocardial function using the criteria of Ross and Braunwald (15). This patient, age 57, had a resting CI of 2.82 liters/min per m^2, a mean PA pressure of 24 mm Hg and an arterial oxygen saturation of 86%, values much less abnormal than those of several other patients with COPD. Although this single abnormal response remains unexplained, it would not be surprising if one of 16 male patients in this age group had coronary artery disease of such hemodynamic significance that impairment of left ventricular function might occur under the stress of an increased afterload.

The results of this study should not be interpreted as indicating that COPD never depresses left ventricular function. It is indeed possible, if not likely, that severe hypoxia and acidosis which develop during episodes of acute respiratory insufficiency could impair the functional ability of the myocardium at that time. However, if this does occur, it is highly unlikely that it leads to chronic impairment of left ventricular function. Each of the patients in Group C3 had been admitted to the hospital on more than one occasion (range 2–5) for episodes of acute respiratory insufficiency with

acidosis, yet a normal left ventricular response was observed in each of these patients. Also the subsequent course of these patients makes it improbable that the lung disease was not of the severity necessary to produce chronic left ventricular dysfunction. Four of the six patients died of respiratory insufficiency with right ventricular failure within 7–23 months of the time of this study. Postmortem examination revealed marked right ventricular hypertrophy in all, and the left ventricle appeared normal in three. Left ventricular hypertrophy was described in the remaining patient although measurements of wall thickness were not made. This latter finding has been observed in a significant percentage of these patients by several investigators (2–7), although it has not been a universal finding (23). If left ventricular hypertrophy does occur as a result of COPD, it would appear from the present study that this compensatory mechanism is sufficient to maintain normal left ventricular performance in these patients.

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