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THE EFFECTS OF MITRAL VALVULOPLASTY ON CARDIOVASCULAR AND RENAL FUNCTION AT REST AND DURING EXERCISE¹

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The effects of mitral valvuloplasty on general cardiohemodynamic function in patients with mitral stenosis have been reported by many investigators (1-10). Measurements of renal blood flow, glomerular filtration rate, and excretion of sodium and their correlation with changes in cardiac output, blood oxygen measurements, and vascular pressures also have been extensively studied in patients with various types of heart disease, with and without congestive failure, at rest (11, 12) and during exercise (13-15). However, little information is available on the changes in renal circulation or excretion of electrolytes and water in the period early after mitral valvuloplasty (16). The purpose of this paper is to describe these changes in renal function and to correlate them with alterations in cardiovascular responses. Particular effort has been made to determine whether a specific cardiohemodynamic pattern is associated with disturbances of salt and water excretion before and after mitral valvuloplasty, both at rest and during exercise.

METHODS AND MATERIALS

Nine patients who had mitral stenosis and, in some instances, minimal aortic valvular disease, were studied before and after mitral valvuloplasty. A complete clinical description of the cardiovascular status and treatment of each of the patients is indicated in Table I. The laboratory procedures were performed before, and from 2 to 32 weeks after the operation.

The patients were studied in the postabsorptive state without any sedative medication. A double-lumen intracardiac catheter was placed in the right heart and pulmonary artery. An inlying needle was maintained in the

brachial artery. Zero point of reference of the pressures was 10 cm. anterior to the back of the patient in the supine position. Pressures were measured by electro-manometers⁴ and recorded by a direct-writing oscillograph. Mean pressures were determined by electrical integration.

The resistances were calculated from the following formulae:⁵

The "total pulmonary" resistance (actually, total resistance opposing the right ventricle) was obtained from the following equation:

$$R = \frac{PA_m}{CO} \times 1,332 \text{ dynes seconds cm.}^{-5}$$

The "pulmonary arteriolar" resistance (actually, the total pulmonary vascular resistance) was calculated as follows:

$$R = \frac{PA_m - "PC_m"}{CO} \times 1,332 \text{ dynes seconds cm.}^{-5}$$

The "total peripheral" resistance (actually, total resistance opposing the left ventricle) was calculated as follows:

$$R = \frac{BA_m \times 1,332}{CO} \text{ dynes seconds cm.}^{-5}$$

⁴ Sanborn Company, Cambridge, Massachusetts.

⁵ Vascular resistances were calculated according to formulae devised by Gorlin and his co-workers (17), whose designations are employed here. "Total pulmonary" resistance is defined in terms of the gradient of pressure from the pulmonary arteries to zero, and actually includes the resistance of the pulmonary vessels, that of the mitral valve, as well as the resistance to filling by the left ventricle. Thus, the so-called "total pulmonary" resistance should more correctly be designated as the total resistance opposing the right ventricle. Similarly, calculation of the "pulmonary arteriolar" resistance is based on the pressure gradient between the pulmonary arteries and the "wedge-pressure." If the latter reflects pulmonary venous pressure, then the calculation of "pulmonary arteriolar" resistance actually includes the resistance of the capillaries and venules, and should be called total pulmonary vascular resistance. "Total peripheral" resistance, furthermore, is calculated on the basis of the pressure drop from the large arteries to zero, and actually includes the resistance to filling by the right heart. Therefore, this should more correctly be defined as the total resistance opposing the left ventricle.

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The work of the right and left ventricles against pressure was calculated with the following formulae:

$$W_R = \frac{(CI \times 1.055)([PA_m - RA_m] \times 13.6)}{1,000}$$

kg. M. per minute per M²,

$$W_L = \frac{(CI \times 1.055)([BA_m - 5] \times 13.6)}{1,000}$$

kg. M. per minute per M²,

PA_m = pulmonary arterial mean pressure in mm. Hg,

"PC_m" = "pulmonary capillary" mean pressure in mm. Hg,

BA_m = brachial arterial mean pressure in mm. Hg,

CO = cardiac output in ml. per second,

1,332 = factor for converting mm. Hg to dynes per cm.²,

W_R = work of right ventricle against pressure,

W_L = work of left ventricle against pressure,

CI = cardiac index, liters per minute per M²,

RA_m = right atrial pressure in mm. Hg,

1,055 = specific gravity of blood,

5 = assumed left ventricular diastolic pressure in mm. Hg,

13.6 = specific gravity of mercury.

An indwelling catheter was placed in the urinary bladder. After standard priming doses, a sustaining infusion containing inulin (3.3 per cent) and para-amino-hippurate (0.5 per cent) in 3.5 per cent glucose and water was started and given at the rate of 1.2 ml. per minute by means of a calibrated drip.

After a preliminary practice run, at least one and usually two resting cardiac output determinations were made by the direct Fick method. Expired air was collected for two minutes in a Douglas bag while simultaneous blood samples were obtained at a constant rate from the brachial and pulmonary arteries. Immediately before and after the Fick procedure, pressures in the pulmonary artery, right ventricle, and brachial artery were recorded. The resting "pulmonary capillary" pressure was measured after the completion of measurement of the resting cardiac outputs. The volume of inspired air was measured by a Tissot spirometer which supplied outdoor air to the patient. Oxygen and carbon dioxide concentrations in the expired air were determined by the Haldane method (18), duplicate determinations being required to agree within 0.03 vol. per cent. Blood samples were analyzed for oxygen content, capacity and saturation by the method of Van Slyke and Neill (19). Blood oxygen contents were corrected for differences in hematocrit, duplicate determinations being required to agree within 0.10 vol. per cent.

During the control period, three to four urine collections were obtained. Urine was collected at the end of each 10 to 15-minute period by washing out the bladder with 20 ml. of distilled water and evacuating the residual urine by displacement with air. Every twenty minutes arterial blood samples were obtained for the determinations of inulin, para-amino hippuric acid, chloride, sodium, potassium, and hematocrit. Blood and urine concentrations of para-amino hippuric acid were measured by the method of Goldring and Chasis (20) and inulin was determined by the method of Schreiner (21) or Roe, Ep-

stein, and Goldstein (22). Serum and urinary sodium and potassium were determined by the internal standard flame photometer (lithium). Serum and urinary chloride were analyzed by the method of Wilson and Ball (23). Hematocrit was measured in Wintrobe tubes.

Measurements during the effects of exercise were carried out as follows:

With the distal lumen of the catheter wedged in a radicle of the pulmonary artery the patient exercised in the supine position by alternate straight leg-raising from two and one-half to nine and one-half minutes. During the final minute of exercise the cardiac output was measured. At the instant that the exercise was stopped the measurements of brachial artery, "pulmonary capillary," pulmonary arterial, and right ventricular pressures which were being taken were recorded for use in the calculation of the hemodynamic data. (Pressure measurements were also taken and recorded repeatedly during exercise but were not regarded as completely valid because of the marked fluctuations in intrathoracic and intra-abdominal pressures associated with the strenuous exercise of alternate straight leg-raising.) Urine collections were made at the end of the 10-minute period including the time during which the exercise was performed ("the exercise period") and thereafter for three 10 to 15-minute periods. All these procedures were performed after operation in the identical manner as before.

RESULTS

Cardiohemodynamic data for each patient are presented in Table II, and the results in two cases are shown graphically in Figures 1 and 2. The mean data for the group and a statistical analysis are shown in Table III, which is the major basis for the following presentation.

Cardiovascular responses

Cardiac index and oxygen measurements. The mean resting cardiac index for the entire group before the operation was 2.71 liters per minute per square meter of body surface. The mean increase in the resting cardiac index for the group after operation was 0.36 liter per minute per square meter of body surface, which was not statistically significant. The mean cardiac index during exercise was 0.76 L. per min. per M² greater after than before operation. In response to exercise all but one patient (C. J.) had rises in cardiac index both before and after operation (average 0.87 L. per min. per M² preoperatively and 1.26 L. per min. per M² postoperatively). Thus, the response of cardiac index to exercise after operation averaged 0.41 L. per min. per M² greater than

TABLE I
Clinical data of the patients before and after mitral valvuloplasty

Symptoms and signs of congestive failure																
Patient Age Sex	Clinical classifi- cation	Hemo- pysis	Dysp- nea	Veins	Rates	Liver below costal margin cm.	Periph- eral edema	Rhythm*	Treatment		Ven- tricular hyper- trophy by EKG	Arterial hyper- tension	Valvular lesions (according to clinical and surgical findings)*		Calcifi- cation mitral valve	
									Digit- alis	Diu- salt retic diet†			M.S.†	M.I. A.S. A.I.		
J. C. M	IV Pre-op.	4+	4+	3+	2+	4	1+	AF	+	+	R	0	4+	1+	0	4+
43	III Post-op.	0	1+	2+	0	0	0	AF	+	+	R	0	2+	1+	0	4+
A. L. F	III Pre-op.	0	4+	2+	2+	0	1+	AF	+	+	0	0	4+	0	0	0
36	III Post-op.	0	1+	2+	0	0	0	AF	+	+	0	0	2+	0	0	0
C. J. F	IV Pre-op.	0	4+	4+	2+	6	4+	AF	+	+	R	+	4+	0	0	2+
40	III Post-op.	0	2+	2+	0	2	0	AF	+	+	R	0	3+	0	0	2+
C. S. M	III Pre-op.	0	4+	2+	1+	0	1+	NSR	+	+	R	0	4	0	0	1+
37	I Post-op.	0	0	0	0	0	0	NSR	0	0	R	0	1+	0	0	1+
E. M. F	III Pre-op.	0	4+	0	0§	0	0	NSR	+	+	0	+	4+	0	0	0
48	III Post-op.	0	2+	0	0	0	0	NSR	+	+	0	+	2+	0	0	0
C. M. M	III Pre-op.	0	4+	0	0	0	0	NSR	0	0	0	0	3+	0	0	0
49	II Post-op.	0	1+	0	0	0	0	NSR	0	0	0	0	1+	0	0	0
E. T. F	III Pre-op.	4+	4+	0	0§	0	0	NSR	+	0	0	0	4+	0	0	0
22	II Post-op.	0	1+	0	0	0	0	NSR	+	0	0	0	1+	0	0	0
E. C. F	III Pre-op.	2+	4+	2+	0	4	1+	AF	+	0	0	0	4+	0	0	0
50	II Post-op.	0	1+	0	0	0	0	AF	+	0	0	0	1+	0	0	0
A. C. M	II Pre-op.	0	3+	0	0	0	0	NSR	0	0	0	0	4+	0	0	0
40	I Post-op.	0	0	0	0	0	0	NSR	0	0	0	0	1+	1+	0	0
A. S. F	III Pre-op.	4+	3+	0	0	0	0	NSR	+	0	0	0	4+	0	0	0
39	III Post-car- diotomy	4+	2+	0	0	0	0	NSR	+	0	0	0	4+	0	0	0

* Key to abbreviations:

AF = Auricular Fibrillation.
NSR = Normal Sinus Rhythm.

R = Right.

M.S. = Mitral Stenosis.

M.I. = Mitral Insufficiency.

A.S. = Aortic Stenosis.

A.I. = Aortic Insufficiency.

† <3 gm. NaCl per day.

‡ Surgical estimation of length of mitral valvular orifice.

1+ = >3.1 cm.

2+ = 2.1-3 cm.

3+ = 1.1-2 cm.

4+ = 0.5-1 cm.

§ Attacks of pulmonary edema occurred in these patients.

TABLE II
Individual cardiohemodynamic data *

Patient Age	Sex	Body surface area (M ²)	Time relative to operation	Arterial oxygen saturation %		Oxygen consumption ml./min./M ²		A-V oxygen difference vol. %		Cardiac index L./min./M ²		Heart rate beats/min.		Stroke index ml./beat/M ²	
				R	E	R	E	R	E	R	E	R	E	R	E
43	J. C.	M	Pre-op.	91	90	163	347	5.23	10.69	3.18	3.23	85	100	37	32
	1.99														
	1.96		16 wks. Post-op.	94	95	164	350	5.07	8.48	3.26	4.12	66	98	49	42
36	A. L.	F	Pre-op.	99	100	148	427	5.86	10.67	2.54	4.00	84	180	30	22
	1.64														
	1.63		9 wks. Post-op.	97	99	144	427	5.03	10.48	2.85	4.07	92	140	31	29
40	C. J.	F	Pre-op.	89	86	180	209	9.04	10.92	1.98	1.91	107	124	18	15
	1.63														
	1.57		2 wks. Post-op.	92	95	182	321	6.24	11.46	2.93	2.80	84	98	35	29
37	C. S.	M	Pre-op.	93	90	179	427	6.73	13.36	2.67	3.19	85	136	31	23
	1.64														
	1.71		28 wks. Post-op.	98	98	171	439	4.13	7.45	4.17	5.89	80	110	52	54
48	E. M.	F	Pre-op.	89	86	127	—	5.66	9.71	2.24	—	77	104	29	—
	1.66														
	1.63		20 wks. Post-op.	95	93	131	363	4.80	9.35	2.74	3.88	71	120	39	32
49	C. M.	M	Pre-op.	100	92	130	367	4.21	7.51	3.09	4.89	63	98	49	50
	1.69														
	1.69		32 wks. Post-op.	99	99	125	379	5.04	9.06	2.48	4.19	60	84	41	50
22	E. T.	F	Pre-op.	94	92	146	377	4.42	8.24	3.28	4.58	62	110	53	42
	1.49														
	1.48		17 wks. Post-op.	99	—	144	357	3.75	6.65	3.86	5.36	78	96	50	56
50	E. C.	F	Pre-op.	95	100	130	280	6.22	11.13	2.14	2.51	48	88	44	28
	1.43														
	1.44		2 wks. Post-op.	96	94	149	344	5.12	9.41	2.87	3.65	82	100	35	37
40	A. C.	M	Pre-op.	96	94	145	470	4.45	9.83	3.25	4.79	78	138	42	35
	2.10														
	2.08		6 wks. Post-op.	94	94	124	538	4.97	10.65	2.48	5.06	68	120	36	42
39	A. S.†	F	Pre-op.	97	99	160	286	4.59	7.84	3.49	3.65	84	112	42	33
	1.46														
	1.46		16 wks. Post-op. (Cardiotomy)	96	98	172	425	4.67	7.99	3.67	5.29	79	128	46	41

* R = Rest
E = Exercise
S = Systolic
D = Diastolic
M = Mean

† Not included in mean or statistical summary.
M²—refers to square meters of body surface area.

TABLE II—*Continued*

Patient Age Sex Body surface area (M ²)	Time relative to operation	Pressures (mm. Hg)															
		Pulmonary artery						Mean "pulmonary capillary"		Right ven- tricular end diastolic		Systemic arterial					
		R			E							R			E		
		S	D	M	S	D	M	R	E	R	E	S	D	M	S	D	M
43 J. C. 1.99 M	Pre-op.	90	45	55	115	55	85	22	32	10	15	120	70	85	145	80	95
1.96	16 wks. Post-op.	58	28	40	80	40	53	20	30	12	15	130	75	90	160	100	120
36 A. L. 1.64 F	Pre-op.	35	20	24	63	40	43	21	30	15	30	140	90	110	178	110	130
1.63	9 wks. Post-op.	33	15	22	48	30	37	14	27	10	12	130	75	90	187	115	140
40 C. J. 1.63 F	Pre-op.	125	70	90	175	80	115	25	35	25	—	190	120	150	200	135	160
1.57	2 wks. Post-op.	78	40	52	110	52	72	19	35	12	26	120	80	100	170	115	125
37 C. S. 1.64 M	Pre-op.	102	47	65	138	61	99	30	41	10	18	130	80	100	170	100	135
1.71	28 wks. Post-op.	50	28	38	80	48	60	22	30	5	10	120	60	90	145	70	100
48 E. M. 1.66 F	Pre-op.	76	38	55	110	52	75	34	55	5	10	170	90	120	265	150	207
1.63	20 wks. Post-op.	47	28	35	88	48	57	28	42	5	12	190	100	130	210	110	145
49 C. M. 1.69 M	Pre-op.	65	30	40	112	52	85	26	55	5	10	135	75	100	180	90	130
1.69	32 wks. Post-op.	32	16	23	60	35	45	15	22	5	5	125	65	90	145	75	110
22 E. T. 1.49 F	Pre-op.	45	20	33	82	46	65	20	40	2	5	105	60	80	125	72	88
1.48	17 wks. Post-op.	42	22	32	58	30	43	18	36	5	5	122	62	79	—	—	—
50 E. C. 1.43 F	Pre-op.	50	30	40	90	55	68	20	38	10	15	105	60	75	—	—	—
1.44	2 wks. Post-op.	53	28	35	86	40	56	18	21	8	10	100	60	75	105	65	80
40 A. C. 2.10 M	Pre-op.	45	35	40	90	60	68	30	48	5	20	138	80	100	140	80	100
2.08	6 wks. Post-op.	33	20	25	58	38	47	15	21	5	10	140	90	110	160	90	120
39 A. S.† 1.46 F	Pre-op.	50	28	35	70	34	50	18	28	5	10	120	70	95	155	90	120
1.46	16 wks. Post-op. (Cardiotomy)	45	23	33	75	38	55	20	30	4	9	130	80	100	—	—	—

TABLE II—Continued

Patient Age	Sex	Body surface area (M ²)	Time relative to operation	Resistances <i>dynes seconds cm⁻⁵</i>				Work of ventricles against pressure <i>kg. M./min./M²</i>					
				"Total pulmonary"		"Pulmonary arteriolar"		Total peripheral		Right ventricle		Left ventricle	
				R	E	R	E	R	E	R	E	R	E
43	J. C.	M	Pre-op.	700	1,050	420	660	1,080	1,180	2.0	3.3	3.6	4.2
	1.99												
	1.96		16 wks. Post-op.	500	520	250	230	1,130	1,190	1.3	2.2	4.0	6.8
36	A. L.	F	Pre-op.	460	520	60	160	2,110	1,580	0.3	0.8	3.8	7.2
	1.64												
	1.63		9 wks. Post-op.	380	450	140	120	1,550	1,690	0.5	1.5	3.5	7.9
40	C. J.	F	Pre-op.	2,230	2,950	1,610	2,050	3,710	4,100	1.8	—	4.1	4.2
	1.63												
	1.57		2 wks. Post-op.	900	1,310	570	670	1,740	2,270	1.7	1.8	4.0	4.8
37	C. S.	M	Pre-op.	1,190	1,510	640	890	1,830	2,060	2.1	3.7	3.6	6.0
	1.64												
	1.71		28 wks. Post-op.	430	480	180	240	1,010	790	2.0	4.2	5.1	8.0
48	E. M.	F	Pre-op.	1,180	—	450	—	2,580	—	1.6	—	3.7	—
	1.66												
	1.63		20 wks. Post-op.	630	720	130	190	2,320	1,830	1.2	2.5	4.9	7.8
49	C. M.	M	Pre-op.	610	820	210	290	1,530	1,260	1.6	5.3	4.2	8.8
	1.69												
	1.69		32 wks. Post-op.	440	510	150	260	1,720	1,240	0.6	2.4	3.0	6.3
22	E. T.	F	Pre-op.	540	760	210	290	1,310	1,030	1.4	3.9	3.5	5.4
	1.49												
	1.48		17 wks. Post-op.	450	430	200	70	1,110	—	1.5	2.9	4.4	—
50	E. C.	F	Pre-op.	1,050	1,510	520	670	1,960	—	0.9	1.9	2.3	—
	1.43												
	1.44		2 wks. Post-op.	680	850	330	530	1,460	1,220	1.1	2.4	2.9	4.2
40	A. C.	M	Pre-op.	470	540	120	160	1,170	800	1.6	3.3	4.4	6.5
	2.10												
	2.08		6 wks. Post-op.	390	360	160	200	1,710	910	0.7	2.7	3.7	8.3
39	A. S.†	F	Pre-op.	550	750	270	330	1,490	1,800	1.5	2.1	4.5	6.0
	1.46												
	1.46		16 wks. Post-op. (Cardiotomy)	490	570	190	260	1,490	—	1.5	3.5	5.0	—

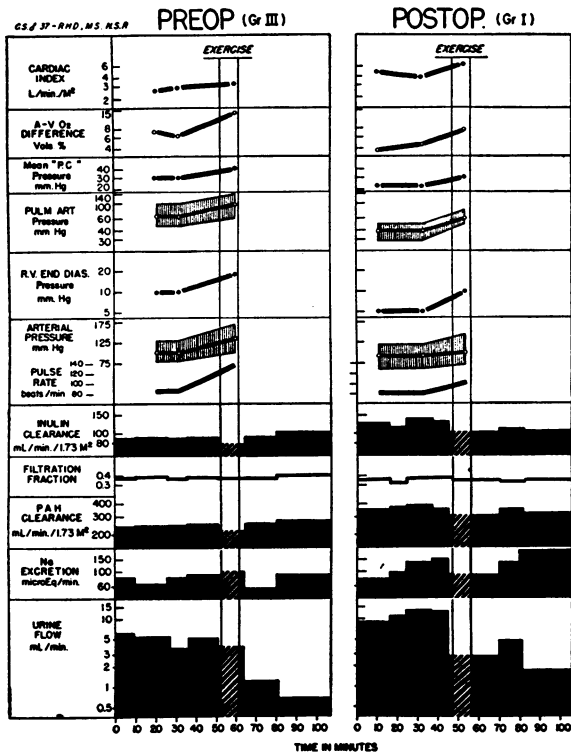


FIG. 1. CHART OF THE CARDIOVASCULAR AND RENAL MEASUREMENTS AT REST AND DURING EXERCISE IN PATIENT C. S. WITH MITRAL STENOSIS BEFORE AND AFTER MITRAL VALVULOPLASTY

Postoperatively this patient showed the greatest improvement in cardio-renal function both at rest and during exercise.

before operation, but this change lacked statistical significance.

The oxygen consumption of each patient at rest was almost identical before and after operation. With exercise the oxygen consumption tended to be higher after than before operation, perhaps reflecting ability to do a greater amount of work. This difference lacked statistical significance in the group as a whole. The arterio-venous oxygen differences both at rest and during exercise were on the average about 1 vol. per cent lower after operation than before. The range of the data was so wide, however, that for this small group statistical analysis did not indicate the change to be significant. The arterial oxygen saturation of seven of the nine patients decreased slightly with exercise preoperatively, but this occurred in only two patients postoperatively. Statistically these changes were not significant. However, in this part of the oxygen dis-

sociation curve small differences in saturation may represent considerable differences in oxygen tension, which we did not measure directly.

Vascular pressures

Pulmonary arterial pressure. All of the patients had abnormally elevated pulmonary arterial pressures at rest both before (average 49 mm. Hg) and after operation (average 34 mm. Hg), this change being physiologically and statistically highly significant ($P = 0.01$). After exercise, the average mean pulmonary arterial pressure was 78 mm. Hg before operation and 52 mm. Hg after operation. All of the patients had a lower mean pulmonary arterial pressure in response to exercise after than before operation, the

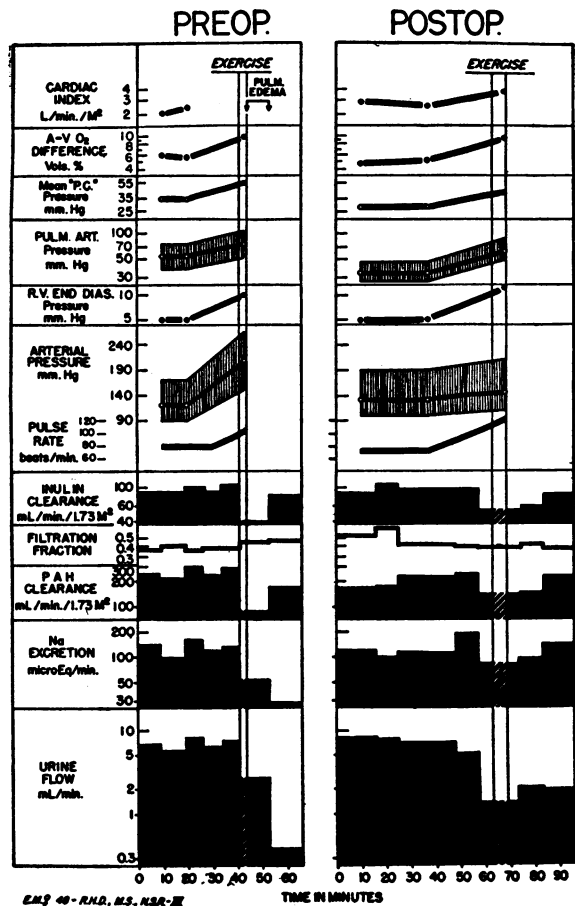


FIG. 2. CHART OF THE CARDIOVASCULAR AND RENAL MEASUREMENTS AT REST AND DURING EXERCISE IN PATIENT E. M. WITH MITRAL STENOSIS BEFORE AND AFTER MITRAL VALVULOPLASTY

Preoperatively the patient developed pulmonary edema during exercise.

decrease being 6 to 43 mm. Hg (average 26 mm. Hg). In response to exercise, the mean pulmonary arterial pressure rise averaged 29 mm. Hg (59 per cent) before operation and 19 mm. Hg (56 per cent) after operation. All these changes had high physiologic and statistical significance.

"Pulmonary capillary" pressure. The average mean "pulmonary capillary" ("PC") pressure at rest before operation was 25 mm. Hg and 19 mm. Hg after operation. Postoperatively six of the

nine patients showed a significant fall in mean pressures at rest (6 to 15 mm. Hg). In none of these patients, however, did the mean pressure return to normal. In response to exercise the mean "PC" pressure rose, on the average, to 42 mm. Hg preoperatively and 29 mm. Hg postoperatively, or an average of 13 mm. Hg lower after operation, a change which was highly significant statistically. However, the average rise in mean "PC" pressure after exercise was 16 mm.

TABLE III
Mean data and statistical analysis

A. Cardio-vascular	Arterial oxygen saturation %			Oxygen consumption ml./min./M ²			A-V oxygen difference vol. %		
	R	E	Response to exercise	R	E	Response to exercise	R	E	Response to exercise
Mean pre-op.	94.0±1.3	92.0±2.8	-1.8±1.2	150±7	363±30	+210±33	5.76±0.50	10.23±0.57	+4.47±0.46
Mean post-op.	96.0±0.8	96.0±1.7	+0.2±0.6	148±7	391±22	+243±26	4.90±0.24	9.22±0.52	+4.32±0.32
Mean diff.*	+2.0±1.0	+3.6±1.9	+2.0±1.6	-2±4	+31±16	+34±16	-0.85±0.41	-1.01±0.74	-0.16±0.63
P	0.08	0.1	0.2	0.6	0.09	0.07	0.08	0.2	0.8

A. Cardio-vascular	Cardiac index L./min./M ²			Heart rate beats/min.			Stroke index ml./beat/M ²		
	R	E	Response to exercise	R	E	Response to exercise	R	E	Response to exercise
Mean pre-op.	2.71±0.16	3.64±0.39	+0.87±0.26	77±6	120±9	+43±8	37±4	31±4	-7±2
Mean post-op.	3.07±0.20	4.34±0.31	+1.26±0.25	76±3	107±6	+32±5	41±2	41±4	+0.3±2
Mean diff.*	+0.36±0.24	+0.76±0.35	+0.41±0.19	-1±6	-12±6	-12±7	+4±4	+12±3	+8±3
P	0.2	0.07	0.07	0.9	0.09	0.1	0.3	<0.01	0.033

Pressures (mm. Hg)												
A. Cardio-vascular	Mean pulmonary artery			Mean "pulmonary capillary"			Right ventricular end diastolic			Mean systemic arterial		
	R	E	Response to exercise	R	E	Response to exercise	R	E	Response to exercise	R	E	Response to exercise
Mean pre-op.	49±7	78±7	+29±3	25±2	42±3	+16±2	10±2	15±3	+8±2	102±8	131±15	+25±10
Mean post-op.	34±3	52±4	+19±1	19±1	29±2	+10±1	7±1	12±2	+4±1	95±6	118±7	+21±5
Mean diff.*	-15±4	-26±4	-10±3	-6±1	-13±4	-6±3	-2±2	-6±2	-5±2	-7±6	-14±12	-5±16
P	<0.01	<0.01	<0.01	<0.01	0.015	0.1	0.2	0.049	0.032	0.3	0.3	0.7

Resistances dynes seconds cm ⁻⁵									
A. Cardio-vascular	"Total pulmonary"			"Pulmonary arteriolar"			Total peripheral		
	R	E	Response to exercise	R	E	Response to exercise	R	E	Response to exercise
Mean pre-op.	940±190	1210±280	+300±80	470±160	650±220	+170±50	1920±280	1720±420	-100±130
Mean post-op.	530±60	630±100	+90±40	230±50	280±70	+40±30	1530±140	1390±180	-190±150
Mean diff.*	-400±140	-590±180	-210±40	-240±120	-360±170	-130±50	-390±240	-480±350	-50±170
P	0.021	0.015	<0.01	0.08	0.1	0.042	0.2	0.2	0.7

Work of ventricles against pressure kg. M./min./M ²						
A. Cardio-vascular	Right ventricle			Left ventricle		
	R	E	Response to exercise	R	E	Response to exercise
Mean pre-op.	1.5±0.2	3.2±0.5	+1.8±0.4	3.7±0.2	6.0±0.7	+2.2±0.6
Mean post-op.	1.2±0.1	2.5±0.3	+1.3±0.2	3.9±0.3	6.8±0.5	+2.9±0.4
Mean diff.*	-0.3±0.2	-0.6±0.5	-0.2±0.1	+0.2±0.3	+0.9±0.7	+0.9±0.6
P	0.1	0.2	0.1	0.5	0.3	0.1

TABLE III—Continued

B. Renal	Clearance ml./min./1.73 M ²							
	PAH				Inulin			
	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery
Mean pre-op.	318 ± 31	195 ± 31	-138 ± 22	294 ± 35	100 ± 7	64 ± 10	-38 ± 12	102 ± 8
Mean post-op.	370 ± 47	283 ± 51	- 87 ± 11	351 ± 42	117 ± 10	90 ± 14	-26 ± 6	129 ± 12
Mean diff.	+42 ± 38	+82 ± 47	- 56 ± 26	+48 ± 43	+16 ± 9	+24 ± 22	+12 ± 16	+14 ± 11
P	0.3	0.1	0.08	0.3	0.1	0.3	0.5	0.3

B. Renal	F.F. %				UV ml./min.				U _{Na} V MicroEq./min.			
	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery
	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery
Mean pre-op.	33 ± 2	34 ± 5	+2 ± 3	36 ± 3	4.8 ± 1.1	1.7 ± 0.5	-4.0 ± 0.9	2.5 ± 1.3	107 ± 17	62 ± 11	-45 ± 17	101 ± 39
Mean post-op.	34 ± 1	34 ± 2	+0.3 ± 2	34 ± 3	6.7 ± 1.4	2.9 ± 0.6	-4.0 ± 1.3	3.6 ± 0.9	125 ± 23	86 ± 18	-40 ± 11	121 ± 20
Mean diff.	+1 ± 2	0 ± 3	-2 ± 4	0 ± 3	—	—	0.2 ± 1.8	—	—	—	- 4 ± 14	—
P	0.5	—	0.6	—	—	—	>0.9	—	—	—	0.8	—

B. Renal	U _K V MicroEq./min.				U _{Cl} V MicroEq./min.			
	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery
	Rest	Exercise	Response to exercise	Recovery	Rest	Exercise	Response to exercise	Recovery
Mean pre-op.	52 ± 7	34 ± 4	-19 ± 7	52 ± 7	80 ± 16	60 ± 10	- 32 ± 16	82 ± 21
Mean post-op.	68 ± 11	43 ± 8	-24 ± 8	63 ± 7	126 ± 20	92 ± 16	- 34 ± 10	125 ± 18
Mean diff.	—	—	- 7 ± 8	—	—	—	-0.2 ± 13	—
P	—	—	0.4	—	—	—	>0.9	—

* In occasional cases, measurements of some variables were available preoperatively but not postoperatively, or *vice versa*. These are included in the mean pre- and postoperative data. Occasional discrepancies between the means, the individual differences, and the difference between average pre- and postoperative values for the group are due to inclusion of these occasional unpaired data.

Hg (64 per cent) before, and 10 mm. Hg (53 per cent) after operation, a change which was not statistically significant. However, in three patients the rise in "PC" pressure following exercise was considerably lower (12 to 22 mm. Hg) after operation.

Right ventricular end-diastolic pressure. The average right ventricular end-diastolic (R.V.D.) pressure at rest before operation was 10 mm. Hg and after operation 7 mm. Hg. After exercise the average R.V.D. pressure was 15 mm. Hg preoperatively and 12 mm. Hg postoperatively. In response to exercise the R.V.D. pressure increased on the average 8 mm. Hg before operation and only 4 mm. Hg after operation, a change which was just statistically significant.

Arterial pressure, heart rate, stroke index

The average mean arterial pressure at rest, 102 mm. Hg preoperatively and 95 mm. Hg postoperatively, showed no significant change. However, postoperatively two patients, A. L. and C. J. (the latter patient having associated arterial hy-

pertension) showed appreciable falls in the mean arterial pressure of 20 and 50 mm. Hg, respectively. Likewise, the response of the arterial pressure to exercise was not significantly different before and after operation.

The heart rate at rest was 77 beats per min. preoperatively and 76 beats per min. postoperatively for the group, while after exercise it was 120 beats per min. before and 107 beats per min. after operation. Similarly, in response to exercise the heart rate was, on the average, 12 beats per min. lower after operation. These changes were not statistically significant.

At rest the slight rise in the stroke index after operation was not significant. However, with exercise the average stroke index was 31 ml. per min. per M² preoperatively and 41 ml. per min. per M² postoperatively. Likewise, the increase in stroke index in response to exercise was on the average 8 ml. per min. per M² more after than before operation. These increases in stroke index were significant and reflected the associated increases in cardiac index and reductions in heart rate after operation.

Vascular resistances (in units of dynes seconds cm^{-5})

The "total pulmonary" resistance, which includes the calculated resistance of the mitral valve itself, is normally under 200 units at rest. Postoperatively there was a considerable and statistically significant decrease in this resistance as calculated from the data obtained during rest, the average declining from 940 to 530 units. The resistances thus remained elevated above normal even after operation. The resistances calculated from the measurements obtained following exercise likewise dropped (on the average from 1,210 to 630 units) after operation, which is also highly significant statistically. While some patients had only negligible changes in resistance as a result of operation, the direction of the change was uniformly downward.

In response to exercise, "total pulmonary" resistance in normal subjects usually decreases. In eight patients in whom data were obtained both at rest and after exercise pre- and postoperatively, the resistance rose considerably following exercise. The average rise was, however, much less after operation (90 units) than before (300 units). This change was highly significant statistically.

"Pulmonary arteriolar" resistance at rest is normally up to 100 units, and it usually decreases with exercise. In this group, the highly elevated preoperative resting value (average 470 units) declined after operation to 230. Following exercise the "pulmonary arteriolar" resistance was increased (average 650 units) preoperatively, and declined to 280 units after operation. Although most of the patients had lower "pulmonary arteriolar" resistances both at rest and following exercise after operation, the average decreases for the entire group lacked statistical significance. However, the average increase in "pulmonary arteriolar" resistance in response to exercise was 170 units before operation and was only 40 units after operation, a reduction which was statistically significant.

The above calculated resistances indicate that about half the decrease in resistance opposing the right ventricle, both at rest and after exercise, can be accounted for in terms of a reduction in the resistance of the pulmonary vessels, and the other half in terms of a lessening of the resistance beyond the lungs, namely of the mitral valve itself.

The "total peripheral" resistance after operation tended to be less at rest and following exercise than before operation, but these changes were small and not statistically significant.

Ventricular work against pressure (in units of $\text{kg. M. per min. per M}^2$)

The work of the right ventricle against pressure (normally less than 1.0 unit) was abnormally high at rest preoperatively (1.5 units) and declined postoperatively to 1.2 units. With exercise, the average right ventricular work rose to 3.2 units preoperatively and to only 2.5 units postoperatively. Thus, the considerable decrease in pulmonary arterial pressure with operation tends to reduce the amount of work by the right ventricle to a greater degree than the slight rise in cardiac output that acts to increase it. As a result of the balances of these two factors, the net effect is a reduction in the right ventricular work, but one which is not statistically significant.

The work of the left ventricle against pressure at rest tended to rise slightly after operation because the increase in cardiac output was greater than the fall in peripheral arterial pressure. However, neither the average values of the left ventricular work at rest nor the responses to exercise after operation were significantly greater than before operation.

Renal responses before and after mitral valvuloplasty

Individual renal data are presented in Table IV, and group means and their statistical analysis in Table III.

At rest. Preoperatively all the patients had an abnormally low renal plasma flow (average 318 ml. per min. per 1.73 M^2) while five patients (C. S., E. M., C. M., E. C., A. C.) also had lower than normal glomerular filtration rates (mean value for the entire group was 100 ml. per min. per 1.73 M^2). Although after operation the renal plasma flow and glomerular filtration rate at rest showed significant increases to or towards normal in three patients, C. S., E. T., E. C., the postoperative renal plasma flow (mean 370 ml. per min. per 1.73 M^2) and glomerular filtration rate (mean 117 ml. per min. per 1.73 M^2) for the group as a whole did not show a statistically significant increase. Since intake of dietary salt was not regu-

lated, the influence of the operation upon the excretion of electrolytes at rest could not be accurately evaluated.

During exercise. During the exercise period the mean renal plasma flow was 195 ml. per min. per 1.73 M² preoperatively and 283 ml. per min. per 1.73 M² postoperatively. Before operation the renal plasma flow decreased in response to exercise, on the average, 138 ml. per min. per 1.73 M² or 43 per cent, and the glomerular filtration rate fell, on the average, 38 ml. per min. per 1.73 M², or 38 per cent. After operation, exercise produced only about half as much decrease in the renal plasma flow (mean reduction 87 ml. per min. per 1.73 M², or 23 per cent), but this alteration just lacked statistical significance for the group. Likewise, the glomerular filtration rate was low-

ered only half as much after operation (mean reduction 26 ml. per min. per 1.73 M², or 22 per cent), but again the change lacked statistical significance for the group.

Preoperatively, associated with the reduction caused by exercise in renal plasma flow and glomerular filtration rate, there were decreases in urine flow and the excretion of sodium, and usually of chloride, except in one patient, C. S. Likewise, after operation in all but one patient, J. C., there was a decrease in sodium excretion during the exercise period. In general, except for patient E. T., the reduction in sodium excretion during the exercise period paralleled the fall in the renal plasma flow and glomerular filtration rate. However, in response to exercise the decrease in sodium excretion was not significantly different be-

TABLE IV
Individual renal data

Patient Age	Sex	Body surface area (M ²)	Time relative to operation	Procedure	Periods	C _{PAH} ml./min./ 1.73 M ²	C _{IN} ml./min./ 1.73 M ²	F.F. %	UV ml./min.	U _{Na} V MicroEq./ min.	U _{Cl} V MicroEq./ min.	U _K V MicroEq./ min.
43	M	1.96	16 wks. Post-op.	Control	1-5	451	124	28	11.0	132	126	52
				Exercise 6 min.	6	336	100	30	5.5	142	138	39
				Recovery	7-9	384	113	29	6.0	166	180	56
36	F	1.64	Pre-op.	Control	1-5	330	114	35	10.0	121	87	35
				Exercise 7 min.	6	229	97	42	2.7	67	75	35
				Recovery	7-9	306	115	38	10.0	282	170	64
			9 wks. Post-op.	Control	1-4	305	121	40	12.0	131	128	45
				Exercise 9½ min.	5	189	84	44	5.2	61	78	32
40	F	1.63	Pre-op.	Control	1-3	347	—	—	2.5	96	95	75
				Exercise 5 min.	4	124	—	—	0.15	33	40	24
				Recovery	5-6	283	—	—	0.91	63	76	60
			2 wks. Post-op.	Control	1-3	378	—	—	3.2	56	83	111
				Exercise 5 min.	4	290	—	—	1.3	24	28	34
37	M	1.64	Pre-op.	Control	1-4	256	95	37	5.0	80	73	39
				Exercise 8 min.	5	220	82	37	3.9	102	101	44
				Recovery	6-7	267	104	39	0.94	74	59	41
			28 wks. Post-op.	Control	1-4	381	131	34	11.0	116	98	88
				Exercise 9½ min.	5	318	106	33	2.8	89	97	63
48	F	1.66	Pre-op.	Control	1-5	267	98	37	7.0	127	79	35
				Exercise 2½ min.	6	94	42	44	2.7	54	36	17
				Recovery	7	181	83	46	0.40	29	33	27
			20 wks. Post-op.	Control	1-4	215	101	47	7.3	132	119	37
				Exercise 6 min.	5	146	55	37	1.4	84	84	22
				Recovery	6-7	199	87	38	2.1	119	114	49

TABLE IV—Continued

Patient Age	Sex	Body surface area (M ²)	Time relative to operation	Procedure	Periods	C _{PAH} ml./min./ 1.73 M ²	C _{IN} ml./min./ 1.73 M ²	F.F. %	UV ml./min.	U _{Na} V MicroEq./ min.	U _{Cl} V MicroEq./ min.	U _K V MicroEq./ min.
49	M	1.69	Pre-op.	Control	1-5	381	106	28	5.8	170	150	79
				Exercise	6	236	75	32	1.1	83	66	44
				8 min.								
				Recovery	7-8	430	124	29	3.9	130	114	77
		1.69	32 wks.	Control	1-3	303	91	30	1.9	135	158	77
			Post-op.	Exercise	4-5	255	84	32	2.4	94	123	67
				7 min.								
				Recovery	6	291	100	34	3.5	107	137	88
22	F	1.49	Pre-op.	Control	1-3	486	127	26	4.5	47	64	51
				Exercise	4	324	36	11	0.43	34	41	27
				6½ min.								
				Recovery	5-6	392	115	29	0.41	28	42	37
		1.48	17 wks.	Control	1-3	689	169	25	1.0	85	67	16
			Post-op.	Exercise	4	634	165	26	0.48	70	54	16
				5 min.								
				Recovery	5-6	625	173	28	0.34	81	64	22
50	F	1.43	Pre-op.	Control	1-3	206	82	40	0.28	6	12	35
				Exercise	—	—	—	—	—	—	—	—
				Recovery	—	—	—	—	—	—	—	—
		1.44	2 wks.	Control	1-4	368	127	35	6.3	286	266	106
			Post-op.	Exercise	5	269	94	35	4.9	192	181	84
				7 min.								
				Recovery	6-8	385	125	33	2.5	226	216	77
40	M	2.10	Pre-op.	Control*	1-3	268	76	28	3.4	780	778	66
				Exercise	4	140	54	39	0.80	204	216	44
				7 min.								
				Recovery	5-7	197	69	35	1.0	221	242	56
		2.08	6 wks.	Control	1-4	242	72	29	6.6	51	85	79
			Post-op.	Exercise	5	108	36	33	2.5	14	41	34
				8 min.								
				Recovery	6-8	225	84	37	4.4	27	55	76
39	F	1.46	Pre-op.	Control	1-3	589	121	20	4.7	148	120	35
				Exercise	—	—	—	—	—	—	—	—
				Recovery	—	—	—	—	—	—	—	—
		1.46	16 wks.	Control	1-3	513	133	26	11.0	148	105	31
			Post-op.	Exercise	4	265	78	29	0.08	21	17	11
			(Cardiotomy)	6 min.								
				Recovery	5	355	110	31	0.20	7	8	15

* Patient was given 300 ml. 5 per cent NaCl I.V.

fore and after operation. The significant decrease in the excretion of potassium during exercise both before and after operation tended to parallel the changes in the glomerular filtration rate. The magnitude of the decrease in the excretion of potassium in response to exercise was not significantly different preoperatively and postoperatively.

Recovery from exercise. Persistently lower values of glomerular filtration rate and renal plasma flow lasting from 13 to 45 minutes after exercise were observed in four patients (A. C., C. J., E. M., and E. T.) before operation. Two of these patients (E. M. and E. T.) developed clinical pulmonary edema during exercise. Three other patients (A. L., C. S., C. M.), none of whom developed pulmonary edema, had a prompt restor-

ation in the renal hemodynamic measurements after exercise and a return to control values within 22 to 45 minutes. Postoperatively, the renal plasma flow tended to return more rapidly and completely to the pre-exercise values during the same period of recovery.

Before operation all except two patients (A. L., C. S.) had reductions in sodium, chloride and usually water excretion during exercise which *persisted* during the recovery period. In the recovery phase sodium and water retention in most of the patients appeared to be independent of the changes in the glomerular filtration rate, since the latter measurements frequently had already returned to the control values. After operation all patients recovered more readily from the exercise-

induced reductions of sodium excretion except for three patients (E. C., C. M., A. C.) who had a persistent decrease in sodium excretion after exercise.

DISCUSSION

There was no consistent relationship between the cardiohemodynamic and the renal functional abnormalities observed in these patients before or after operation. No correlation could be found to exist between the absolute levels of the cardiac output and the renal plasma flow and glomerular filtration rate at rest or during exercise. After mitral valvuloplasty three patients (C. S., E. T., E. C.) showed significant increases in renal plasma flow at rest, and four (C. J., E. M., C. M., E. T.) had smaller decreases in renal plasma flow during exercise. Of the two patients (C. S., E. T.) who had appreciable increases in the glomerular filtration rate at rest, one (E. T.) had a smaller decrease in the glomerular filtration rate in response to exercise after operation. However, these changes in renal plasma flow and glomerular filtration rate were not invariably related to improvement in cardiac output. For example, one patient in the group (C. S.) who had the greatest increase in cardiac output in response to exercise postoperatively had a fall in the renal hemodynamic measurements equal to that found preoperatively. On the other hand, the cardiac output response to exercise was similar before and after operation in patient C. J. whereas the renal plasma flow during the exercise period showed a lesser fall after than before operation.

Prior to operation two patients (E. M., E. T.) developed cardiac asthma during exercise with markedly elevated "pulmonary capillary" pressures, and also had marked reductions in glomerular filtration rate and renal plasma flow and persistent decreases in the excretion of salt and water. After operation they had no cardiac asthma with exercise and smaller decreases in renal plasma flow, glomerular filtration rate, or excretion of salt and water. However, the decreases in renal plasma flow and glomerular filtration rate during the exercise period in the group as a whole could not be correlated with any abnormal increases in mixed arteriovenous oxygen difference or levels of central vascular pressures before or after operation.

Preoperatively the return of the renal hemodynamic measurements to or towards control levels after the exercise period was not consistently related to the prior increase in cardiac output during exercise. However, in some patients after operation there appeared to be an association between improvement in the cardiac output responses to exercise and speed of return of the renal hemodynamic measurements to control levels after exercise. In several patients before operation the decreases in the excretion of sodium and water persisted for some time after exercise. In some cases they continued after the glomerular filtration rates had returned to control values. These decreases were therefore attributed, at least in part, to increased renal tubular reabsorption of salt and water. After operation, however, these decreases in renal function in general persisted for shorter periods. In only one patient (A. C.) in whom an increased renal tubular reabsorption of sodium persisted after exercise did a marked increase in the hematocrit (suggesting a decrease in blood volume with hemoconcentration) occur during exercise both before and after mitral valvuloplasty. It is possible that these two factors may have directly influenced the renal tubular reabsorption of sodium. In other patients during exercise, smaller increases in hematocrit occurred and appeared to contribute little, if at all, to the retention of sodium.

None of the patients after operation had a return to normal of their cardiohemodynamic or their renal functions in response to exercise. Several patients, on the other hand, had a return of individual functions to or almost to normal values at rest. In some, the reductions in urine flow, sodium excretion, renal plasma flow, and glomerular filtration rate were less marked especially in response to exercise than before operation. Likewise in some, the cardiohemodynamic abnormalities were less marked both at rest and in response to exercise than before operation. However, there was no consistent parallelism between these two types of improvement, particularly if measurements of only a single renal or circulatory function was considered. However, there was a fairly consistent trend for those patients with the more normal cardiohemodynamic responses to exercise to show the more normal renal responses.

In general, symptomatic improvement paralleled

improvement in the cardiohemodynamic, or the renal function, or both. However, in some patients marked subjective improvement was noted with little change in either the cardiovascular or renal measurements. In fact, one patient (A. S.) in whom the left auricle was opened but no fracture of the mitral valve accomplished because of technical difficulties had marked symptomatic improvement for about six months without any significant alterations in cardiovascular or renal function.

Some reports on physiologic data obtained from patients with mitral stenosis following mitral valvuloplasty indicate that maximum improvement in the hemodynamic measurements may not appear immediately (24), or early, but usually several months after operation (25-27). The hemodynamic observations in our patients, who were studied early after operation (2 to 32 weeks), were believed at the time to represent maximum states of improvement. Cardiac catheterizations have been repeated in a majority of them one and one-half to two years postoperatively, and the hemodynamic responses in some cases found to be more normal and in others more abnormal than the initial postoperative studies reported here, and a few, actually more abnormal than the preoperative values (28).

SUMMARY

Cardiovascular and renal measurements were made at rest and following exercise in nine patients with mitral stenosis before and within 2 to 32 weeks after mitral valvuloplasty. Cardiohemodynamic measurements after operation showed a slight, but not statistically significant, increase in the cardiac index, and a significant increase in the stroke index, since the heart rates tended to be slower. The pulmonary arterial and "pulmonary capillary" pressures were significantly lower. The right ventricular end-diastolic pressure was not significantly reduced at rest, but after exercise it was significantly less than before operation. The calculated "total pulmonary" resistance (which includes the resistance imposed by the mitral valve) was significantly reduced, but the "pulmonary arteriolar" resistance was not. The increase in the "pulmonary arteriolar" resistance in response to exercise was not so great after operation. The resistance opposing the right ventricle

was decreased after operation apparently because of approximately equal reductions in the resistance of the pulmonary vessels and that imposed by the stenosis of the mitral valve. There was a slight reduction in the work of the right ventricle and a slight increase in the work of the left ventricle after operation but neither was statistically significant.

Preoperative resting renal plasma flow was approximately half and glomerular filtration rate about four-fifths of normal values. After operation the resting renal plasma flow and glomerular filtration rate were both increased, on the average, by about one-sixth, the latter approaching normal. In response to exercise the renal plasma flow fell, on the average, 43 per cent before operation and only one-half that much after operation, a significant improvement. The glomerular filtration rate decreased in response to exercise, on the average, 38 per cent before operation and only about two-thirds that much after operation. This improvement was not statistically significant. The considerable decreases in urine flow, excretion of sodium, chloride and potassium in response to exercise, which tended to parallel the changes in the glomerular filtration rate, were not significantly different in magnitude after operation as compared with before. Although all the renal functions tended to recover from exercise more rapidly after operation, the mean data showed no significant differences from the preoperative responses.

In this group of patients mitral valvuloplasty produced varying degrees of improvement in the cardiovascular and renal functions both at rest and after exercise. In none of the patients, however, did the cardio-renal hemodynamic measurements return to normal values. A general improvement in cardiovascular function in individual patients was sometimes associated with increases in renal plasma flow, glomerular filtration rate and the ability to excrete salt and water during and after exercise. However, postoperative increases in salt and water excretion could not be consistently correlated with any specific change in cardiovascular or renal function, or both.

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