Exercise haemodynamics of coarctation of the aorta

Acute effects of propranolol¹

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Eight patients with aortic coarctation were studied at rest and during supine bicycle exercise before and after intravenous propranolol 0.17 mg./kg. The mean pressure gradient across the aortic narrowing increased from 16 to 45 mm. Hg during exercise, and was reduced to 11 and 31 mm. Hg after propranolol. Total peripheral resistance was increased by propranolol both at rest and during exercise, and the diminished pressor response was due to a 20 per cent decrease in exercise cardiac output. Brachial artery systolic pressure was reduced more than central aortic systolic pressure in 2 of the 3 patients in whom both pressures were monitored. In one patient descending aortic pressure fell during exercise; in the remainder, slight increases were noted.

The increase in arterial blood pressure proximal to the obstruction in patients with aortic coarctation may be due to mechanical, renal, or additional factors (Shepherd, 1963). Some patients with coarctation show increments in the upper extremity arterial blood pressure with moderate physical exercise (Taylor and Donald, 1960), but exercise descending aortic pressures have not been the subject of study. In order further to investigate the raised exercise blood pressure, 8 patients with coarctation of the aorta were studied at rest and during supine bicycle exercise, monitoring both ascending and descending aortic pressures.

The accentuated pressor response to exercise in patients with coarctation may be due to the mechanical effect of an increase in the rate of left ventricular ejection into an aorta with a limited run-off capacity. As the rate of left ventricular ejection may be reduced by beta-adrenergic inhibition (Cumming and Carr, 1967), the exercise haemodynamics of coarctation of the aorta were restudied after the intravenous administration of propranolol.

Patients

Data on the patients are given in Table 1. Case 7 was a woman, the others were men or boys. The mean age was 14 years and the mean work load on

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the bicycle was 325 kpm./min. The mean dose of propranolol was 0.17 mg./kg. The diagnosis in all patients was proven by aortography. Operation was subsequently performed in Cases 1 to 6, and in 5 of the subjects the aortic lumen was only 1-2 mm. at the site of maximum constriction. In Case 1, the opening was 4 mm. in diameter. The coarctation in Case 7 was mild and operation was not recommended. Case 8 had an operation for coarctation seven years previously, and was restudied because of a persisting difference between arm and leg blood pressure and an accentuated pressor response to exercise.

Methods

Side-hole catheters were inserted into the right ventricle or pulmonary artery from the right arm. In Cases 2, 3, and 5 brachial artery pressure was monitored. In Cases 1 and 4 ascending aortic pressures were measured through side-hole catheters inserted by brachial artery cutdown. In Cases

TABLE 1 Patients with coarctation of aorta

Case No.	Age (yr.)	Height (cm.)	Weight (kg.)	Work load (kpm.)	Propranolol dose (mg.)	Propranolol dose (mg./kg.)
1	14	154	48.1	500	10.0	0.21
2	9	128	25.0	200	5.0	0.20
3	11	132	26.5	300	5.0	0.19
4	14	162	50.8	300	8.0	0.16
5	24	173	68.2	500	10.0	0.15
6	11	160	44.1	300	8.0	0.18
7	19	164	56.4	200	8.0	0.14
8	13	160	44.5	300	7.0	0.16
Means	14	154	45.4	325	7.6	0.17
SD	± 5	± 16	± 14.4	± 117	± 1.9	± 0.02

6, 7, and 8 ascending aortic pressures were measured through No. 6 or No. 7 Teflon catheters inserted percutaneously through the femoral artery and advanced through the area of aortic constriction into the ascending aorta. During exercise these catheters were withdrawn into the descending aorta to complete the exercise measurements. Descending aortic pressures were not obtained in Cases 2 and 3, and were measured by retrograde aortic catheterization in Cases 1, 4, and 5.

Pressures were recorded with Statham P23DB transducers. Cardiac output was measured with indocyanine green dye, using the dynamic calibration method of Shinebourne, Fleming, and Hamer (1967a). The subjects performed supine exercise on an electronically braked ergometer (Holmgren and Mattsson, 1954). Exercise measurements were obtained during the third to fifth minute of exercise at 60 r.p.m. After 5 minutes of recovery, propranolol was given as a single bolus through the pulmonary artery catheter, and the measurements were repeated 5 to 10 minutes later at rest and with a similar exercise load.

Results

The changes of flow and resistance are indicated in Table 2. For technical reasons cardiac output was not obtained in Case 1. Exercise under control conditions caused the following mean changes: cardiac output increased from 5.3 to 9.0 l./min., heart rate increased from 92 to 138 beats/min., stroke volume increased from 58 to 66 ml./beat, systolic ejection period was shortened from 0.27 to 0.23 sec., the mean rate of left ventricular ejection increased from 209 to 300 ml./sec., and total peripheral resistance fell from 1.30 to 0.95 units.

After propranolol the mean resting cardiac output was reduced by 13% and exercise output was reduced by 20%, changes similar to those found in normal subjects (Cumming and Carr, 1966). Resting heart rate was reduced by 12% and exercise heart rate was reduced by 17%, so that the decreases in cardiac output after propranolol were primarily due to changes in heart rate, with stroke volume showing no significant change. The mean systolic ejection period was prolonged by 0.01 sec. both at rest and during exercise after propranolol. The total peripheral resistance expressed in resistance units (mm.Hg/ml. flow per sec.) was 15% higher at rest and 20% higher on exercise after propranolol. There was no significant change in the mean rate of left ventricular ejection comparing the propranolol and control results.

The pressure measurements are presented in Table 3. Under control conditions exercise increased the mean of the pressures above the coarctation from 145/84 to 188/106 mm. Hg

and the mean of the pressures below the coarctation from 102/78 to 112/83 mm. Hg. Exercise increased the mean aortic pressure gradient from 16 to 45 mm. Hg and the peak gradient from 36 to 76 mm. Hg.

After propranolol there were no significant changes in the mean resting pressure, though the pressures below the coarctation tended to be higher and the mean aortic gradient was reduced from 16 to 11 mm. Hg. After propranolol the exercise pressures above the coarctation were lower by 22/9 mm. Hg, and the mean aortic pressure gradient decreased from 45 to 31 mm.

Discussion

During exercise large increases may occur in the systolic blood pressure of many patients with aortic coarctation, some of whom have nearly normal resting arterial pressures. This is an easily demonstrated finding in clinical practice that does not require special instrumentation. Taylor and Donald (1960) found that 6 of 20 coarctation patients developed brachial artery systolic pressures in excess of 300 mm. Hg with moderate exercise, and concluded that exercise systolic blood pressure was higher in patients with aortic coarctation than in those with other forms of hypertension, despite the higher mean resting pressures in the latter. Part of the increase in systolic pressure with exercise has been attributed to the loss of volume of functioning aortic reservoir and its windkessel effect. The large increase in the systolic brachial artery pressure during exercise in patients with aortic coarctation may also be due to an accentuation of the normal arterial pressure changes during exercise. Rowell *et al.* (1968) have shown that in normal subjects the central aortic systolic pressure increase is much less than peripheral artery systolic pressure during exercise, the difference being due to the standing and reflected wave changes and the technical factors related to the recording methods. In Cases 6, 7, and 8, ascending aortic and peripheral artery pressures were monitored simultaneously during exercise (Table 4). In Case 6 peripheral artery and aortic systolic pressures were within a few millimetres of one another. In Cases 7 and 8 peripheral artery systolic pressure exceeded aortic systolic pressure by 5 to 13 mm. at rest, and by 14 to 40 mm. during exercise, while mean pressures were equal. The differences between the peripheral artery and aortic systolic pressures were considerably reduced by propranolol in these two patients. In Cases 2, 3, and 5, peripheral artery pressures were used to indicate proxi-

TABLE 2 Flow and resistance measurements in patients with coarctation of aorta

Case No.		Cardiac output (l./min.)		Heart rate (beats/min.)		Stroke vol. (l./min.)		Systolic ejection period (sec.)		Total peripheral resistance (mm. Hg/ml. per sec.)		LV ejection (ml./sec.)	
		Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise	Rest	Exercise
1	C	—	—	102	146	—	—	0.28	0.22	—	—	—	—
	P	—	—	88	120	—	—	0.29	0.25	—	—	—	—
2	C	4.3	6.1	106	148	37	41	0.22	0.19	1.81	1.48	168	216
	P	4.2	5.0	97	136	43	37	0.24	0.22	1.71	1.72	179	168
3	C	4.1	8.9	75	136	54	66	0.30	0.24	1.62	0.86	180	275
	P	3.2	5.9	68	115	48	51	0.31	0.25	2.00	1.27	155	203
4	C	6.5	10.1	89	137	73	74	0.28	0.24	1.04	0.91	261	308
	P	5.3	10.0	78	112	67	89	0.28	0.25	1.53	0.86	239	356
5	C	5.6	9.8	92	148	61	67	0.28	0.20	1.36	1.00	208	335
	P	4.7	7.1	84	104	56	68	0.29	0.21	1.62	1.34	193	324
6	C	4.7	8.5	84	148	36	57	0.27	0.21	1.40	0.94	207	271
	P	4.1	7.6	80	116	51	66	0.28	0.25	1.49	0.96	182	264
7	C	5.9	10.3	100	124	59	83	0.30	0.28	0.95	0.69	196	296
	P	5.6	7.0	80	108	70	65	0.30	0.28	1.07	0.94	233	232
8	C	6.0	9.2	84	120	71	77	0.25	0.23	0.91	0.77	240	400
	P	4.9	7.7	72	108	68	71	0.28	0.24	1.14	0.88	175	320
Means	C	5.3 ± 0.9	9.0 ± 1.4	92 ± 11	138 ± 11	58 ± 12	66 ± 14	0.27 ± 0.03	0.23 ± 0.03	1.30 ± 0.35	0.95 ± 0.14	209 ± 32	300 ± 57
	P	4.6 ± 0.8*	7.2 ± 1.6	81 ± 9*	115 ± 10*	57 ± 6	64 ± 16	0.28 ± 0.02*	0.24 ± 0.02*	1.50 ± 0.32*	1.14 ± 0.32*	194 ± 31	267 ± 90

C, control; P, propranolol. * $p < 0.05$.

mal aortic pressures, probably producing an overestimation of the aortic systolic gradient, but not affecting the mean gradient.

In patients with aortic coarctation the effects of exercise on the pressure gradients across the narrowing have not been previously studied. The change was conspicuous in Case 1; this case had a gradient of only a few millimetres at rest and over 40 mm. during exercise. The exercise change in this boy, who was keen to take part in sports, influenced the decision to recommend surgical resection of the narrow aortic segment despite a normal resting blood pressure. The peak systolic gradient across the aortic narrowing increased from 10 mm. at rest to 75 mm. during exercise in this patient. In the other patients the peak systolic pressure gradients across the narrowing ranged from 21 to 125 mm. during exercise.

The mean aortic pressure distal to the coarctation was increased from 89 at rest to 95 during exercise. In patients with occlusive peripheral vascular disease, arterial pressure distal to the obstruction may fall during exercise, presumably because blood flows rapidly into the dilated vascular bed of the muscle and is not replaced by a corresponding increase in arterial inflow (DeWeese, 1960). In Case 6 in

this series the descending aortic blood pressure decreased during exercise, while in the remainder of the cases slight increases in aortic pressure distal to the coarctation were noted.

Total resistance to aortic outflow in the patients with coarctation was moderately raised at rest, but fell normally with exercise, as it does in patients with essential hypertension (Hamer, 1968).

Intravenous propranolol does not appreciably decrease the resting arterial pressure in normotensive or hypertensive patients (Prichard, 1964). However, the hypertensive overshoot of the Valsalva manoeuvre (Prichard, 1964) and the pressor responses to cyclic (Cumming and Carr, 1967) and sustained (Donald *et al.*, 1967) muscular contractions are attenuated by propranolol, presumably because of the reduced cardiac responses to these stimuli.

Oral propranolol has been reported to lower the resting blood pressure by about 30/25 mm. Hg in hypertensive Europeans (Paterson and Dollery, 1966) but was without effect in hypertensive Jamaicans, suggesting that these subjects were under minimal beta-adrenergic stimulation (Humphreys and Delvin, 1968). Shinebourne *et al.* (1967b) found that oral

TABLE 3 Coarctation of aorta: pressure data (mm. Hg)

Case No.	Condition	Pulmonary artery						Ascending aorta					
		Systole Rest	Exercise	Diastole Rest	Exercise	Mean Rest	Exercise	Systole Rest	Exercise	Diastole Rest	Exercise	Mean Rest	Exercise
1	C	35	64	7 ^V	6	—	—	120	190	82	120	95	143
	P	32	46	8	6	—	—	125	147	85	90	98	109
2	C	18	39	7	10	15	16	170 ^B	200	90	105	130	150
	P	18	34	6	15	12	23	160	180	90	105	120	144
3	C	37	55	15	22	23	33	155 ^B	172	93	100	111	128
	P	41	58	21	28	30	38	150	169	90	103	107	125
4	C	29	—	17	—	20	—	145	185	85	120	115	152
	P	35	—	16	—	22	—	172	178	112	110	135	143
5	C	22	38	8	8	15	22	188 ^B	250	90	105	127	165
	P	19	42	7	16	13	28	176	210	88	103	128	158
6	C	15	23	5	8	10	13	141	190	80	112	110	141
	P	—	34	—	14	—	19	138	152	83	94	102	122
7	C	19	28	9	12	13	18	130	160	80	88	93	118
	P	17	31	6	18	13	24	131	150	80	85	100	110
8	C	20	35	8	20	12	26	107	155	72	98	90	118
	P	30	40	11	18	17	31	115	138	78	82	94	112
Means	C	26	—	11	13	16	21	145	188	84	106	109	139
		±8		±5	±6	±4	±7	±26	±30	±7	±11	±15	±17
	P	27	—	11	18	18	27	146	166	88	97	111	128
		±10		±6	±5*	±7	±7	±22	±24*	±11	±10*	±15	±18*

V = right ventricle. B = brachial artery. * $p < 0.05$. C = control. P = propranolol.

propranolol reduced systolic pressure by 20% and diastolic pressure by 10% during exercise in hypertensive patients. In this study propranolol failed to alter the peripheral resistance, and the pressure changes were secondary to the reduction in cardiac output.

In our patients the total peripheral resistance was increased both at rest and during exercise after the propranolol. Reflecting this the resting descending aortic pressure was higher after propranolol. The observed changes in pressures and resistances after propranolol may be entirely explained on the basis of alterations in cardiac output and have not assisted in elucidating the mechanism of the hypertension. Patients with coarctation tend to have a high resting cardiac index (Taylor and Donald, 1960), and in this regard are similar to patients with renovascular hypertension (Frohlich *et al.*, 1967).

Coarctation of the aorta is managed by operation, and drug therapy for hypertension is rarely required. Some patients fail to achieve normal pressures after an adequate operation, and an abnormal pressor response to exercise may persist. As these patients have

a high incidence of berry aneurysms, there may be a place for the use of beta-adrenergic inhibition to reduce the pressor response to exercise in selected patients.

References

- Cumming, G. R., and Carr, W. (1966). Hemodynamic response to exercise after propranolol in normal subjects. *Canadian Journal of Physiology and Pharmacology*, **44**, 465.
- , and Carr, W. (1967). Hemodynamic response to exercise after beta-adrenergic and parasympathetic blockade. *Canadian Journal of Physiology and Pharmacology*, **45**, 813.
- DeWeese, J. A. (1960). Pedal pulses disappearing with exercise: a test for intermittent claudication. *New England Journal of Medicine*, **262**, 1214.
- Donald, K. W., Lind, A. R., McNicol, G. W., Humphreys, P. W., Taylor, S. H., and Staunton, H. P. (1967). Cardiovascular responses to sustained (static) contractions. *Circulation Research*, **22-21**, Suppl. 1, 15.
- Frohlich, E. D., Ulrych, M., Tarazi, R. C., Dustan, H. P., and Page, I. H. (1967). A hemodynamic comparison of essential and renovascular hypertension: cardiac output and total peripheral resistance: supine and tilted patients. *Circulation*, **35**, 289.
- Hamer, J. (1968). Hemodynamics of hypertension. Editorial. *American Heart Journal*, **76**, 149.
- Holmgren, A., and Mattsson, K. H. (1954). New ergometer with constant work load at varying pedalling

Descending aorta						Mean aortic gradient		Peak systolic gradient		Case No.	Condition
Systole Rest	Exercise	Diastole Rest	Exercise	Mean Rest	Exercise	Rest	Exercise	Rest	Exercise		
110	115	85	85	93	95	2	48	10	75	1	C
120	105	85	75	97	85	1	24	5	42		P
—	—	—	—	—	—	—	—	—	—	2	C
—	—	—	—	—	—	—	—	—	—		P
—	—	—	—	—	—	—	—	—	—	3	C
—	—	—	—	—	—	—	—	—	—		P
83	95	70	77	77	82	38	70	62	90	4	C
123	98	102	77	109	85	26	58	49	80		P
110	125	85	100	102	108	25	57	78	125	5	C
120	125	90	95	110	109	18	49	56	85		P
100	87	78	68	87	77	23	64	41	103	6	C
99	82	83	71	88	75	16	47	39	70		P
110	125	78	80	87	96	6	22	20	35	7	C
115	122	75	80	98	105	2	5	16	28		P
100	125	72	85	86	109	4	9	7	30	8	C
110	117	74	85	92	106	2	6	5	21		P
102	112	78	83	89	95	16	45	36	76	Means	C
± 11	± 17	± 6	± 11	± 8	± 13	± 15	± 24	± 29	± 38		P
114	108	85	81	99	94	11	31	28	54		
± 9	± 16	± 10	± 9	± 9	± 14	± 11*	± 23*	± 23*	± 28*		

rate. *Scandinavian Journal of Clinical and Laboratory Investigation*, 6, 137.

Humphreys, G. S., and Delvin, D. G. (1968). Ineffectiveness of propranolol in hypertensive Jamaicans. *British Medical Journal*, 2, 601.

Paterson, J. W., and Dollery, C. T. (1966). Effect of propranolol in mild hypertension. *Lancet*, 2, 1148.

Prichard, B. N. C. (1964). Hypotensive action of pronethalol. *British Medical Journal*, 1, 1227.

Rowell, L. B., Brengelmann, G. L., Blackmon, J. R., Bruce, R. A., and Murray, J. A. (1968). Disparities between aortic and peripheral pulse pressures induced by upright exercise and vasomotor changes in man. *Circulation*, 37, 954.

Shepherd, J. T. (1963). *Physiology of the Circulation in Human Limbs in Health and Disease*, p. 327. Saunders, Philadelphia.

Shinebourne, E., Fleming, J., and Hamer, J. (1967a). Calibration of indicator dilution curves in man by the dynamic method. *British Heart Journal*, 29, 920.

—, —, and — (1967b). Effects of beta-adrenergic blockade during exercise in hypertensive and ischaemic heart-disease. *Lancet*, 2, 1217.

Taylor, S. H., and Donald, K. W. (1960). Circulatory studies at rest and during exercise in coarctation of the aorta before and after operation. *British Heart Journal*, 22, 117.

TABLE 4 Simultaneous peripheral artery and ascending aortic pressures

Case No.	Condition	Peripheral artery (mm. Hg)	Aorta (mm. Hg)	Peripheral artery systole—aorta systole
6	Rest	138/75 (105)	141/80 (110)	—3
	Exercise	175/85 (120)	172/85 (120)	+3
	Propran., rest	130/70 (98)	138/87 (102)	—8
	Propran., exercise	150/90 (120)	152/94 (122)	—2
7	Rest	135/58 (81)	130/80 (93)	+5
	Exercise	200/80 (116)	160/88 (118)	+40
	Propran., rest	144/76 (105)	131/80 (100)	+13
	Propran., exercise	168/75 (110)	150/85 (110)	+18
8	Rest	114/67 (89)	107/72 (90)	+7
	Exercise	178/84 (112)	140/92 (112)	+38
	Rest	130/72 (87)	120/80 (87)	+10
	Exercise	185/90 (112)	165/100 (112)	+20
	Propran., rest	125/70 (88)	115/78 (94)	+10
	Propran., exercise	152/78 (110)	138/82 (112)	+14