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Research Article

GENERAL HEMODYNAMICS AND SPLANCHNIC CIRCULATION IN PATIENTS WITH COARCTATION OF THE AORTA[1]

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Controversy concerning the general hemodynamic pattern associated with coarctation of the aorta revolves primarily about the genesis of the systemic arterial hypertension, and the nature and distribution of the peripheral arterial resistance. It is generally agreed (2, 3) that both systolic and diastolic blood pressure levels are elevated above the site of constriction and that the systolic elevation is relatively greater than the diastolic, so that a wide pulse pressure is seen. It is further agreed (2, 3) that systolic and mean pressure levels in the femoral artery are lower than in the brachial artery and that femoral pulse pressure is small. Since there is a mean arterial pressure gradient between the proximal and distal portions of the aorta, two important propositions must be considered: a) if peripheral resistance is distributed uniformly throughout the body, there must be a relatively low blood flow rate through the aorta below the constriction; and b) if the blood flow rate is the same through the proximal and distal segment, the total resistance to flow from the distal segment must be relatively low or, conversely, the total resistance to flow from the proximal segment must be relatively high. Previous investigators have attempted to resolve these problems primarily by study of isolated segments of the circulation. Blumgart, Lawrence, and Ernstene (4) found normal arteriolar pressure in the arms and legs and suggested increased total arterial resistance in the upper part of the body. Prinzmetal and Wilson (5) and Pickering (6) supported this hypothesis by demonstrating that blood flow in the upper extremities was not increased. Steele (7) found elevation of femoral arterial diastolic pressure in three patients and felt that this was evidence for a generalized increase in arteriolar tone throughout the body in patients with coarctation of the aorta. He held that the notion of unequal distribution of the peripheral resistance was untenable because of these findings and a review of reports of observations on 217 patients described by other authors. Steele's argument, based on elevated femoral diastolic pressure, has been refuted by Hull (8), Bing and associates (2), and Gupta and Wiggers (9). These authors cite evidence to show that the tendency toward elevated femoral diastolic pressure is caused by damping of the pulse wave by the aortic constriction and the long collateral channels. It must be admitted that this explanation does not exclude the possible presence of generalized vasoconstriction in patients with coarctation. Such a notion might be supported by the work of Harris, Sealy, and DeMaria (3), who found elevated *mean* femoral arterial pressure in some patients. No generalization concerning widespread arteriolar constriction in the lower systemic arterial compartment seems justified in the absence of measurements of blood flow through the distal aorta. It seems unlikely, therefore, that problems regarding the general distribution of peripheral arterial resistance will be resolved completely until the rate of total blood flow through the lower arterial compartment is measured.

The hypertension in the upper arterial compartment has been attributed to a generalized systemic arteriolar constrictor influence such as that in "essential" or renal hypertension. This hypothesis has been advanced largely from the results

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of animal experiments (10–14) in which the production of renal ischemia by chronic aortic constriction has been followed by generalized hypertension. Despite its attractiveness, the analogy which has been drawn between the hypertension of experimental coarctation, experimental renal hypertension, "essential" arterial hypertension in man, and the hypertension associated with coarctation of the aorta in man likewise is not justified. Studies made on the renal circulation in clinical cases, although fraught with disagreement, have not demonstrated renal ischemia consistently. Some investigators (15, 16) have found the renal hemodynamic pattern to be similar to that seen in "essential" arterial hypertension. Others (3, 17), on the contrary, report normal renal plasma flow and glomerular filtration rates, as well as normal tubular mass (17). Some observers (4, 18) have held that the hypertension in the proximal aorta is caused by the mechanical obstruction to blood flow offered by the narrowed segment and the collateral vessels. An analogous form of hypertension can be produced in animals by acute aortic constriction (9, 10, 18–20). The postulation of a mechanical cause for the upper compartment hypertension has not been refuted directly.

Additional hemodynamic observations made on clinical cases of coarctation of the aorta have done little toward settling the controversy regarding the origin of the hypertension. Cardiac output has been found to be normal or increased (2, 21–23). Measurements have demonstrated total oxygen consumption to be normal (24) or increased (21, 25). Some investigators (26–28) have reported normal blood flow in the lower extremities, but others (2) have found it to be markedly diminished. Blood flow in the upper extremities has been reported variously as normal (6, 26, 28), increased (2), and decreased (5). Hafkenschiel, Crumpton, and Moyer (29) found increased cerebral blood flow and normal cerebral vascular resistance. These reports, sometimes conflicting or fragmentary, suggest that the hemodynamic pattern is not the same in all patients with coarctation of the aorta. It is reasonable to suppose that, if hemodynamic observations were made on vascular segments both above and below the coarctation at the same time or under the same experimental conditions in a given patient, more reliable interpretation of circulatory abnormalities might be possible. Therefore, we have studied brachial and femoral arterial pressure, minute volume cardiac output (= pulmonary blood flow rate ≒ total systemic blood flow rate), and the hepatic portal circulation in this manner in each of ten patients, with one exception in each of two of these functions. Additional observations were made on the renal circulation during separate experimental sessions in these ten and in eleven other patients. Summary renal circulatory data on the first ten patients only are included in this report for the purpose of general hemodynamic considerations. The detailed analysis of all our renal studies (30) will be presented in a separate communication.

MATERIAL AND METHODS

The usual criteria (31) for the diagnosis of coarctation of the aorta were present in every one of our ten patients: nine men and one woman (Ahl). None had clinical or laboratory evidence of valvular heart disease or additional congenital cardiovascular disorders. The diagnosis was confirmed at operation in all except Patient Wol, who did not receive surgical treatment; but his clinical and hemodynamic findings were unequivocal.

Experimental observations were made in the early morning with the patients in the fasting state and resting in the supine position. Phasic arterial pressure was measured with a capacitance manometer and registered on a multi-channel direct-writing oscillograph, and mean pressure values were obtained by electrical integration of the manometer output (Sanborn equipment). Great care was taken to establish the zero pressure baseline at the mid-atrial level.

Cardiac output was determined by means of the Fick principle with a catheter tip in the pulmonary artery, according to the method of Cournand and associates (32). Mixed venous blood was obtained from the pulmonary artery through the catheter, and systemic arterial blood was drawn simultaneously from the brachial artery through an indwelling needle. Manometric determinations of blood oxygen content were done as described by Van Slyke and Neill (33). Expired air was collected in a calibrated Tissot-type spirometer, and partial pressure of oxygen in these samples and in room air was measured with a Beckman Model C Oxygen Analyzer, checked periodically with the Haldane apparatus.

Hepatic blood flow was estimated by the method of Bradley, Ingelfinger, Bradley, and Curry (34) with certain modifications. Bromsulfalein was infused at approximately 2.5 mg. per minute per M.^{2} to allow calculation of the hepatic plasma clearance rate of bromsulfalein according to the method standardized by Culbertson and associates (35–38). Twenty minutes were allowed for equilibration after initial priming with 100 mg. of bromsulfalein. A peripheral arterial blood sample was drawn at the end of the equilibration period to establish the

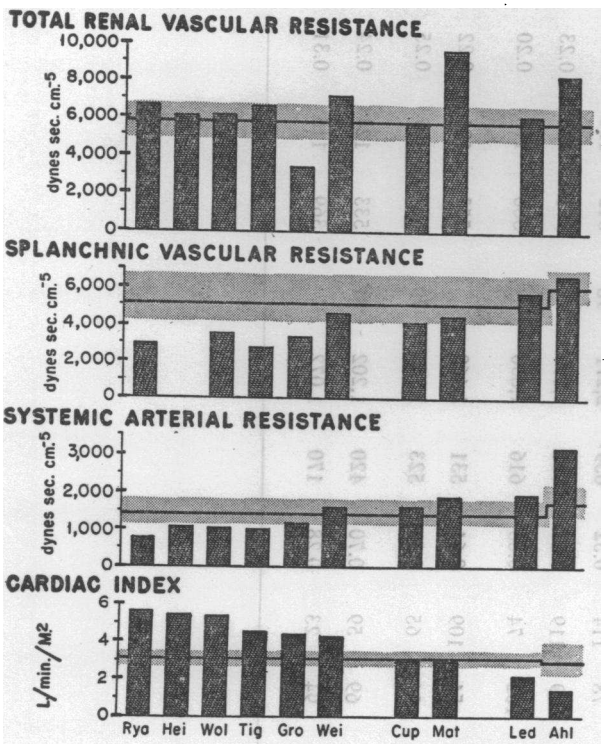

FIG. 1. CARDIOVASCULAR PARAMETERS IN PATIENTS WITH COARCTATION OF THE AORTA

The dark horizontal line in each frame represents an average normal value for that parameter. The width of the horizontal shaded area in the three lower frames is equal to two standard deviations. The offsets between Patients Led (male) and Ahl (female) represent sex differences. The normal values for cardiac index are taken from the observations of Cournand and co-workers (32) on 13 healthy men and six hospitalized women with normal circulatory systems. The normal values for systemic arterial resistance were calculated from the total blood flow data (cardiac index and surface area) from the same source, with an arbitrarily selected heart rate of 60 beats per minute (lower limit of normal)[6] and a mean blood pressure of 100 mm. Hg (average normal). The normal values for splanchnic vascular resistance were calculated in the same way using the data reported by Bradley and co-workers (34) from 18 men and five women, and the same arbitrarily selected pulse rate and blood pressure. The normal values for total renal vascular resistance were calculated according to the method of Gomez (42); the solid line and shaded area represent the average and range (rather than two standard deviations) from nine normal men and one normal woman in our laboratory, averaged without sex distinction.

[6] This tends to minimize the obvious difference between our coarctation patients and normotensive patients. Naturally, the difference between our patients and those with "essential" arterial hypertension is much greater (40). We realize that these are derived figures without the precision suggested by the unit dynes second cm.$^{-5}$ and could be expressed just as usefully as simple units of resistance representing the ratio of pressure to flow as recorded conventionally. The present notation has been used to facilitate comparison with other reported data.

initial peripheral bromsulfalein concentration. Thereafter, four sets of simultaneous peripheral arterial and hepatic venous blood samples were collected at ten-minute intervals. At twenty and at thirty minutes after equilibration simultaneous blood samples were drawn from these sites under oil to derive estimates of the splanchnic oxygen consumption in four of the patients. Bromsulfalein determinations were made on oxalated plasma. Blood volume was estimated from the nomograms of Gibson and Evans (39).

Renal plasma flow (para-aminohippuric acid) and glomerular filtration rate (inulin) were determined by the standard methods of Smith and associates (40–42).

Hemodynamic values were derived to permit comparison of the resistance to blood flow in various regional circuits. These are expressed in dynes cm. second^{-5}. The formulae used were as follows:

$$\text{Resistance to blood flow from the proximal aorta}^{5} = \frac{\text{mean brachial arterial pressure, mm. Hg} \times 1332}{\text{cardiac output, ml. per sec.}};$$

$$\text{Splanchnic vascular resistance} = \frac{\text{mean femoral arterial pressure, mm. Hg} \times 1332}{\text{average estimated hepatic blood flow, ml. per sec.}}.$$

[5] "Systemic arterial resistance" in Figure 1.

Total renal vascular resistance was calculated by the formulae of Gomez (42) and is equal to the sum of the afferent arteriolar, net efferent arteriolar, and venular resistance values. For estimations of splanchnic and renal vascular resistance mean femoral arterial pressure was used, except in the case of Patient Rya, in which mean brachial pressure was applied to the formulae. This obviously resulted in higher than the true values for this patient.

RESULTS

In the figure and tables the ten patients are arranged in order of descending magnitude of the cardiac index. In the first six patients this value was above normal (Figure 1 and Table I). Total oxygen consumption was increased in five patients; and the arteriovenous oxygen difference was diminished in four of these six cases, bearing in general an inverse relationship. The stroke volume cardiac output was elevated both absolutely and in relation to the heart rate in the first five. In the seventh and eighth patients the cardiac index, stroke volume, arteriovenous oxygen difference, and total oxygen consumption were normal. The final two patients were considered to be in

TABLE I

Summary of hemodynamic data

Patient Sex	Age	Surface area	Hematocrit	Brachial arterial pressure		Femoral arterial pressure		Pulmonary "capillary" mean* pressure	Total oxygen consumption rate	Pulmonary A-V oxygen difference	Cardiac index	Heart rate	Stroke volume	Average hepatic BSP extraction fraction	Average plasma BSP clearance rate	Average estimated hepatic blood flow rate	Average rate of splanchnic oxygen consumption	Average effective renal plasma flow rate	Average glomerular filtration rate	Average glomerular filtration fraction
				Phasic	Mean*	Phasic	Mean*													
	yrs.	*M.²*	*per cent*	*mm. Hg*	*mm. Hg*	*mm. Hg*	*mm. Hg*	*mm. Hg*	*ml./min.*	*ml./100 ml.*	*L./min./M.²*	*beats/min.*	*ml.*	*decimal*	*ml./min./1.73 M.²*	*ml./min./1.73 M.²*	*ml./min./1.73 M.²*	*ml./min./1.73 M.²*	*ml./min./1.73 M.²*	*decimal*
Rya M	24	1.94	44.5	155/90	105			11	347	3.2	5.57	52	208	0.67	950	2,568		631	128	0.20
Hei M	19	1.69	36.6	160/95	120	105/75	85		300	3.3	5.38	74	123		758			626	116	0.19
Wol M	44	1.98	44.1	205/100	135	115/80	95	7	339	3.2	5.35	73	145	0.50	538	1,997	86	624	142	0.23
Tig M	18	1.97	43.8	180/80	110	110/75	90	11	346	3.9	4.52	78	114	0.52	659	2,271	98	542	124	0.23
Gro M	18	1.88	44.0	165/90	115	120/75	85	11	288	3.5	4.36	69	119	0.63	651	1,870		971	226	0.23
Wei M	27	1.75	46.4	250/100	150	125/95	105	5	315	4.2	4.29	102	74	0.63	616	1,836		586	116	0.20
Cup M	44	1.93	45.9	165/90	120	105/80	85		265	4.5	3.06	54	109	0.64	531	1,460		553	121	0.22
Mat M	15	1.76	41.2	180/95	125	120/90	100	8	231	4.4	3.01	81	65	0.52	523	1,735	79	422	107	0.25
Led M	28	1.83	49.5	155/75	100	105/85	90	13	211	5.2	2.24	69	59	0.70	420	1,202	81	533	127	0.24
Ahl F	16	1.46	40.6	130/70	90	95/65	75	26	202	9.0	1.50	94	23	0.28	170	1,072		369	115	0.31

* Electrically integrated.

TABLE II

Observed hepatic circulatory and metabolic data *
(not corrected to standard surface area)

Patient and BSP load	Systemic arterial plasma BSP concentration	Hepatic venous plasma BSP concentration	Hepatic venous extraction fraction	Average intravenous infusion rate of BSP	Rate of change in systemic plasma BSP concentration	Estimated plasma volume	Removal rate of plasma BSP	Hepatic plasma BSP clearance rate	Estimated hepatic plasma flow rate	Estimated hepatic blood flow rate	Hepatic arteriovenous oxygen difference	Splanchnic oxygen consumption rate
mg./min./M.²	*mg./100 ml.*	*mg./100 ml.*	*decimal*	*mg./min.*	*mg./L./min.*	*liters*	*mg./min.*	*ml./min.*	*ml./min.*	*ml./min.*	*ml./100 ml.*	*ml./min.*
Rya 2.45	0.45	0.15	0.67	4.76	0.02	3.26	4.77	1,068	1,613	2,906		
Hei 2.34	0.53			3.96	0.01	3.19	3.94	743				
Wol 2.53	0.80	0.41	0.50	5.00	0.08	3.35	4.73	604	1,255	2,244	4.9	96
Tig 2.54	0.68	0.33	0.52	5.00	0.04	3.36	5.08	749	1,450	2,581	4.1	112
Gro 2.66	0.71	0.26	0.63	5.00	0.06	3.19	4.98	708	1,138	2,032		
Wei 2.40	0.71	0.27	0.63	4.20	0.07	2.81	4.40	622	994	1,855		
Cup 2.62	0.92	0.32	0.64	5.05	0.12	3.16	5.35	590	878	1,622		
Mat 2.50	0.80	0.39	0.52	4.40	0.06	3.11	4.26	534	1,040	1,770	4.2	81
Led 2.40	0.99	0.30	0.69	4.40	0.05	2.79	4.39	441	639	1,266	6.3	85
Ahl 2.44	2.32	1.68	0.28	3.56	0.15	2.26	3.31	144	540	909		

* Values for plasma concentration of bromsulfalein, extraction fraction, rate of change, removal rate, and the rates of plasma clearance, plasma flow and blood flow represent the means of four 10-minute observation periods. The infusion rate represents the mean of calculations from a calibrated infusion system drop count made every three minutes during each experiment. Estimated plasma volume is a single reading from the Gibson and Evans nomogram (39). Each value for arteriovenous oxygen difference and oxygen consumption rate is the average of two measurements. A tabular record of all of these original data has been deposited as Document No. 5285 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document No. and by remitting $1.25 for photoprints or for 35 mm. microfilm. Advance payment is required. Make checks or money orders payable to: Chief, Photoduplication Service, Library of Congress.

borderline (Patient Led) or subclinical (Patient Ahl) left ventricular failure on the basis of low cardiac output, normal oxygen consumption, high normal or large arteriovenous oxygen difference and elevated pulmonary "capillary" pressure. Study of these last two cases suggests that subclinical left ventricular failure may have been responsible for some of the discrepancies in values obtained for regional blood flow rates recorded in the literature without accompanying general hemodynamic data on patients with coarctation.

Hepatic blood flow (Tables I and II) was estimated in five of the first six patients and was found to be well above the normal average. The values tended to parallel the general systemic blood flow, as we have found in resting, fasting patients with other circulatory abnormalities (43, 44). The hepatic plasma clearance of bromsulfalein was generally normal, as was the hepatic extraction fraction of bromsulfalein. All of these hepatic circulatory and metabolic values were normal in the seventh and eighth patients but tended to be reduced in Patients Led and Ahl. Splanchnic oxygen consumption (Table I) in general paralleled hepatic blood flow but was not reduced in any of the four patients in whom it was measured.

In the brachial artery the systolic pressure was elevated in all patients not in heart failure, but the diastolic pressure was normal in six and only slightly increased in the remaining four (Table I). Pulse pressure generally was wide, in contrast to the finding in "essential" hypertension uncomplicated by structural arterial disease. Mean pressure was elevated considerably in one patient, moderately in one, and slightly in four; in four patients it was normal. Femoral artery systolic pressure was normal in each of nine recorded cases (not measured in Patient Rya). Femoral diastolic and mean pressure levels were normal, except for Patient Wei, in whom the diastolic pressure was slightly increased. The femoral arterial pulse pressure was characteristically narrow.

Renal plasma flow and glomerular filtration rates (Table I) fell generally within the normal range in the first seven patients. We cannot explain the unusually high values in Patient Gro (in this patient, measurements made at about six months after operation revealed lower but still abnormally high values in spite of a modest fall in cardiac output). A slight elevation in filtration fraction was noted in four of these first seven patients. The renal plasma flow was definitely low in Patient Mat, and there was a distinct increase in his filtration fraction. The renal pattern in the two patients in borderline or subclinical heart failure (Patients Led and Ahl) was characterized by the expected reduced plasma flow, normal glomerular filtration, and increased filtration fraction.

DISCUSSION

If the hypertension in clinical coarctation of the aorta is similar to that observed in "essential" arterial hypertension in man, then all organs and tissues in the body which receive blood from the systemic arterial compartment should share in increased peripheral arteriolar resistance. To refute the argument that the hypertension associated with coarctation of the aorta is similar to "essential" or renal hypertension, the investigator must demonstrate the absence of a generalized increase in the peripheral resistance or show some gross inequality in its distribution.

In seven of our eight patients without evidence of myocardial decompensation the relationship between cardiac output and mean brachial arterial pressure was such that overall resistance to blood flow from the proximal aortic compartment was normal or below normal (Figure 1). A similar pressure-flow relationship was evident in the splanchnic circuit, where not one of nine had an increased arteriolar resistance, in sharp contrast to the finding in "essential" hypertension (45, 46). The situation in the kidney was somewhat different. Renal plasma flow, although generally within normal limits, tended to be relatively low. Because of this, estimates of total renal vascular resistance were relatively high when compared to the hepatic circuit, except for Patient Gro with the renal hyperemia. Of the patients not in heart failure only Patient Mat exhibited a significantly low renal plasma flow. In this case alone the renal vascular resistance approached levels seen in established "essential" hypertension, although splanchnic resistance remained relatively low, in contrast to the characteristic finding in "essential" hypertension.

Our data fail to show increased resistance to blood flow out of the proximal aorta, or through the kidney, or in the splanchnic vascular bed in

patients not in myocardial decompensation. They do indicate that the peripheral resistance has gross inequalities in its distribution in patients with coarctation of the aorta not in congestive heart failure, and that resistance may be decreased or normal in vascular circuits both above and below the constriction in the same patient. There appeared to be a definite tendency for splanchnic vascular resistance to parallel resistance to blood flow from the proximal aortic segment. No such relationship appeared to exist between the renal and the splanchnic circuits, or between the renal circuit and the upper aortic compartment. This suggests that local regulatory mechanisms, rather than a generalized vasoconstrictor influence, are responsible for the distribution of the peripheral resistance, at least with respect to the renal circuit. In no patient, including Patient Ahl, who was in early congestive heart failure, did we find evidence of the generalized increase in arteriolar resistance which characterizes patients with "essential" systemic arterial hypertension.

The demonstration of a wide pulse pressure in the brachial artery, along with an increased stroke volume in the majority of our patients, is similar to the observations of Gupta and Wiggers (9) in dogs. Our findings support their suggestion that the hypertension above the stricture is related to the degree of narrowing, to a foreshortening of the aortic compression chamber, and to an increased stroke volume of the left ventricle. We believe that these observations on pulse pressure and stroke volume, plus those on the unequal distribution of the peripheral resistance, and the evidence against renal ischemia in the majority of our patients form strong evidence against a renal mechanism in the genesis of the upper compartment systemic arterial hypertension seen in coarctation of the aorta.

CONCLUSIONS

1. The hemodynamic pattern associated with coarctation of the aorta in ten patients is in sharp contrast to that observed in "essential" systemic arterial hypertension or renal hypertension in man.

2. The hypertension observed in the upper arterial compartment should be explained on the basis of mechanical factors and local regulatory mechanisms rather than a postulated generalized vasoconstrictor influence.

3. Evidence for renal ischemia was found in only one of eight patients who were free of congestive heart failure; no hepatic ischemia was seen in the nine patients in whom hepatic blood flow was measured, despite the presence of subnormal mean pressure levels in the lower systemic arterial compartment. The tendency was toward splanchnic hyperemia.

4. The demonstration of incipient or subclinical heart failure in two of our ten patients suggests a possible explanation for some of the discrepancies among previously published reports on isolated hemodynamic features of coarctation of the aorta.

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