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Research Article

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DETERMINATION OF THE HEPATIC ARTERIAL BLOOD FLOW AND OXYGEN SUPPLY IN MAN BY CLAMPING THE HEPATIC ARTERY DURING SURGERY

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The function of the hepatic artery has been extensively studied in animals (1–5). Great differences have been found from one species to another (6, 7), and our knowledge of the significance of the arterial blood supply to the human liver is limited mainly to observations of the late effect of occlusion of the hepatic artery (8) or of the portal vein (9, 10). As these events are followed by compensatory changes in the hepatic circulation (11, 12), no definite conclusions regarding the physiological role of the hepatic artery can be made on this basis. It might be expected that acute, transitory interruption of the blood flow through the hepatic artery minimizes this compensation and thus gives a clearer picture of the function of the artery.

METHODS

The eight patients of this study were premedicated in the ward with morphine and atropine, and transferred to the catheterization room, where a Cournand catheter was introduced via a left antecubital vein into one of the major right hepatic veins, and a small polyethylene tube was inserted percutaneously into the left femoral artery. The patient was then taken to the operating theater, where anesthesia (barbiturate, muscle relaxant, and nitrous oxide-oxygen with intubation) was given. Soon afterward an intravenous infusion of sulfobromophthalein (BSP) was started, after a priming dose of 150 mg. The time of this injection was used as reference time.

Immediately after the opening of the peritoneal cavity the hepatic artery was isolated, a clamp was loosely placed around the hepatic artery proper distal to the gastroduodenal and right gastric branches, and a catheter was introduced into the portal vein through a vein in the mesocolon. After these procedures the field was covered, and no further intraperitoneal manipulations were performed during the study. When the determinations of the control period were completed, the clamp on the hepatic artery was closed, and a second series of determinations was performed during the clamping period which lasted on the average 24 minutes.

All three catheters were connected to stopcocks outside the field and regularly flushed with saline containing heparin. Blood samples were drawn simultaneously from the catheters into heparinized syringes after the first 10 ml had been discarded.

In each period five samples (average) were drawn for the determination of BSP concentrations by method I of Winkler, Tygstrup and Munkner (13). In the middle of each period or, in five cases, twice during the clamping period, blood was drawn for the determination of oxygen tension [polarographic method, (14)], oxygen saturation (reflectometry), hemoglobin concentration, hematocrit, serum glutamic-oxalacetic acid transaminase, serum glutamic-pyruvic acid transaminase, lactic acid dehydrogenase, carbon dioxide tension, and pH (15). The oxygen content was calculated from the saturation and the oxygen capacity (derived from the hemoglobin concentration), and the oxygen tension. An average of 400 ml of blood was drawn for these determinations, and the loss was replaced with bank blood during the sampling.

In six cases the pressure was measured in the hepatic vein, portal vein, and femoral artery in each period by means of a Tybjaerg Hansen condenser manometer, the mid-axillary line used as zero.

Calculations. The hepatic blood flow was calculated by the method of Bradley, Ingelfinger, Bradley and Curry (16), with correction for changing BSP levels. No correction was made for the amount of BSP removed with the blood samples. The hepatic blood flow is designated "hepatic venous blood flow," as distinct from the other flow values calculated.

Splanchnic oxygen consumption was calculated by multiplying the hepatic venous blood flow by the difference in arterial and hepatic venous oxygen content.

Mesenteric oxygen consumption (i.e., splanchnic minus hepatic) was determined during the clamping period by multiplying the hepatic venous blood flow in this period by the arterioportal venous oxygen difference. It was assumed that the mesenteric oxygen consumption was not affected by the clamping of the hepatic artery, whereas the mesenteric blood flow might change. Therefore the mesenteric blood flow in the control period was calculated as mesenteric oxygen consumption during the clamping period divided by the arterioportal venous oxygen difference during the control period.

Hepatic arterial blood flow during the control period was determined as the difference between hepatic venous blood flow and mesenteric blood flow.

Hepatic oxygen consumption was determined as the difference between splanchnic and mesenteric oxygen consumption, and the hepatic arterial oxygen supply as the hepatic arterial blood flow multiplied by the arteriohepatic venous oxygen difference.

The assumptions underlying these calculations are discussed below.

From the pressure recordings the following vascular resistances were calculated: the transhepatic (or "end-sinusoidal") resistance as portal-hepatic venous pressure gradient divided by hepatic venous blood flow; the mesenteric resistance as mean arterioportal pressure gradient divided by mesenteric blood flow; and the hepatic arteriolar resistance as mean arterioportal pressure gradient divided by hepatic arterial blood flow. The resistances are expressed as millimeters of mercury per liter of blood per minute.

Material. Age, sex, and body weight of the patients studied are shown in Table I. Patient 1 suffered from gastric carcinoma, probably a malignant ulcer. In Patient 3 laparotomy revealed peritoneal carcinomatosis, secondary to a gastric tumor. In Patient 5 a cholecystectomy was performed because of stones in the cystic duct. The remaining patients had gastric or duodenal ulcers and underwent, as did Patient 1, a subtotal gastrectomy. The liver function tests were normal preoperatively except in Patient 3, in whom serum transaminases were slightly elevated, and in Patient 5 who was slightly jaundiced.

No ill effects of the study on the postoperative course were observed clinically.

RESULTS

Table I shows the hepatic venous blood flow, the oxygen differences, and the splanchnic oxygen consumption from all the experiments.

The hepatic arterial blood flow was on the average 35 per cent of the hepatic venous blood

TABLE I

Hepatic venous blood flow and splanchnic oxygen consumption during surgery in a control period (A), and during clamping of the hepatic artery (B) *

Patient	Age, Sex	Body wt	Period	Hepatic venous blood flow	Oxygen difference		Splanchnic oxygen consumption
					Arterio-hepatic venous	Arterio-portal venous	
	yrs	*kg*	*min*	*ml/min*	*ml/100 ml*		*ml/min*
1	73♂	68	A 93–108	1,358	5.4	3.6	73
			B 108–127	532	9.9	3.2	53
2	52♀	46	A 36– 53	2,239	5.2	1.1	116
			53– 70	751	10.4	2.3	78
			B 70– 82	516	17.0	3.5	88
3	46♀	39	A 35– 79	1,877	5.5	1.9	103
			B 79– 97	1,078	9.7	2.9	105
			97–113	1,160	8.8	2.9	102
4	42♂	57	A 80–100	1,519	5.9	3.6	90
			B 100–115	948	8.5	2.6	81
			115–131	825	8.0	2.3	66
5	59♂	66	A 45– 73	1,997	5.0	2.0	100
			B 73– 83	1,379	9.3	1.4	128
6	31♂	70	A 55– 73	1,341	4.2	1.2	56
			B 73– 89		7.7	1.4	76
			89–101	992	6.8	1.1	68
7	36♂	78	A 63– 83	1,333	7.4	5.1	99
			B 83–101	1,089	8.3	5.1	90
8	59♀	74	A 43– 70	1,312	6.9	4.1	91
			B 70– 81	839	6.8	4.9	57
			81– 92	871	5.6	4.9	49
		Average	A	1,622	5.7	2.8	91
			B	936	9.0	3.0	83

* When two determinations were available in the clamping period their mean was used for calculating the total average.

TABLE II

Calculated values of flow and oxygen consumption

Patient	Hepatic blood flow*			Hepatic arterial O_2		Mesentery		
	Venous, fall	Arterial	Arterial, as % venous blood flow	Supply	Supply as % hepatic O_2 consumption	Blood flow	O_2 consumption	O_2 consumption as % splanchnic O_2 consumption
	ml/min	*ml/min*	%	*ml/min*	%	*ml/min*	*ml/min*	%
1	826	890	65	48	86	468	17	32
2	1,605	630	28	33	33	1,609	18	21
3	758	166	9	9	13	1,711	33	31
4	632	911	60	54	83	608	22	30
5	618	1,032	52	52	64	965	19	15
6	349	308	23	13	31	1,033	13	16
7	244	245	18	18	24	1,088	56	62
8	457	290	22	20	40	1,022	42	65
Average	686	559	35	31	47	1,063	28	34

* B = during clamping of the hepatic artery; A = control period.

flow, but the range was very wide (see Table II). The fall in the hepatic venous blood flow during the clamping of the hepatic artery differed substantially in several cases from the calculated hepatic arterial blood flow; on the average the former was greater—42 per cent of the hepatic venous blood flow, suggesting an average fall of mesenteric blood flow of about 10 per cent during the clamping. The difference, however, is not statistically significant ($p > 0.10$).

The amount of oxygen supplied to the liver by the hepatic artery is roughly proportional to the hepatic arterial blood flow and averages approximately 50 per cent of the hepatic oxygen consump-

TABLE III

Oxygen tension in the femoral artery, hepatic vein, and portal vein in the control period (A) and during clamping of the hepatic artery (B)

Patient	Oxygen tension						Hematocrit, artery	
	Artery		Hepatic vein		Portal vein			
	A	B	A	B	A	B	A	B
	mm Hg		*mm Hg*		*mm Hg*			
1	87	89	27	17	72	81	41	41
2	133	111 123	33	19 10	61	49 42	44	46
3	125	132 128	33	21 22	54	44 44	45	43
4	86	80 74	27	21 22	36	40 41	44	44
5	101	109	36	26	54	66	45	43
6	88	88 90	30	22 23	43	42 42	46	46
7	180	180	33	31	33	32	44	42
8	116	107 116	25	25 28	35	30 21	38	38
Average	115	113	31	23	49	47	43	43
SD	32.1	32.2	3.9	5.2	14.0	17.9		

TABLE IV

Survey of the sulfobromophthalein data, used for calculation of hepatic venous blood flow during the control period and during clamping of the hepatic artery

Patient	Amount infused	BSP concentration: Average in artery		Average change in artery/min		Average arterio-hepatic venous difference	
		A	B	A	B	A	B
	mg/min	*mg/100 ml plasma*		*mg/100 ml plasma*		*mg/100 ml plasma*	
1	3.89	3.90	4.35	−0.009	0.038	0.62	1.04
2	4.05	1.41	2.06	−0.009	0.030	0.36	0.94
3	4.34	2.39	2.79	0.004	0.107	0.39	0.65
4	2.52	2.09	2.58	0.004	0.011	0.34	0.43
5	3.20	0.88	1.02	−0.001	0.011	0.29	0.44
6	3.52	1.35	1.68	0.000	0.023	0.41	0.62
7	4.26	1.65	1.56	−0.019	0.001	0.73	0.73
8	4.34	2.72	3.23	0.027	0.028	0.46	0.68
Average	3.77	2.05	2.41	0.000	0.020	0.45	0.69

tion. The mesenteric oxygen consumption is on the average 34 per cent of the total splanchnic oxygen consumption. The average reduction in splanchnic oxygen consumption (10 per cent) during the clamping of the hepatic artery is not statistically significant.

The repeated determinations performed during the clamping period in five patients showed no consistent variation in hepatic and portal oxygen extraction.

The arterial oxygen tension, shown in Table III, depended largely on the anesthesia; it varied greatly from case to case, but in each particular patient it was fairly constant during the study. The arterial carbon dioxide tension was uniformly low (on an average 24 mm Hg, SD 5 mm), and the arterial pH correspondingly high (7.55, SD 0.06), owing to hyperventilation during the anesthesia; but no great variations occurred. The oxygen tension in the hepatic veins was significantly reduced during the clamping of the artery.

The BSP infusion rates and plasma concentrations are shown in Table IV. The infusion rates were kept comparatively low in order to avoid too steeply rising concentrations during the clamping. There was no significant difference between the concentrations of arterial and portal venous blood.

The level in serum of transaminases and lactic acid dehydrogenase showed only small and insignificant changes during the operations. In Patient 4 the serum transaminases increased to ten times the normal value on the first postoperative day, gradually declining toward normal values in the course of the following week.

Table V demonstrates the pressure readings and the calculated vascular resistances.

TABLE V

Mean pressure in the femoral artery, hepatic vein, and portal vein in the control period and during clamping of the hepatic artery

Patient	Mean pressure: Artery		Hepatic vein		Portal vein		Resistance: Trans-hepatic		Mesenteric		Hepatic arteriolar
	A	B	A	B	A	B	A	B	A	B	A
	mm Hg		*mm Hg*		*mm Hg*		*mm Hg/L blood flow*				
3	108	116	3	4	8	6	1.1	1.9	105	112	63
4	80	87	7	8	10	10	2.3	2.3	130	94	92
5	105	108	3	6	8	8	2.5	1.5	120	75	83
6	85	105	−1	6	0	9	0.8	3.0	80	100	360
7	98	100	8	7	10	15	1.6	7.6	85	88	379
8	113	108	8	11	15	14	5.3	3.5	93	112	337
Average	98	104	5	7	9	10	2.3	3.3	102	97	219

DISCUSSION

Because of the inaccessibility of the hepatic vessels and the complexity of the hepatic vasculature, atraumatic and direct methods for the determination of the hepatic arterial blood flow have not yet been discovered.

The present method is traumatic, and it is not known to what extent the values are influenced by the anesthesia (e.g., the low Pco_2) and the opening of the peritoneal cavity. These procedures might explain why the hepatic venous blood flow and splanchnic oxygen consumption are on the average a little higher than the values usually stated as normal. The pressures measured in the control period are, however, within the limits found in intact subjects.

Furthermore, the method is indirect and therefore subject to methodological errors which may come into play at several points. The probable errors in the determination of hepatic blood flow by means of BSP have been discussed by Bradley (17). Some of these may be increased when large changes in flow take place; also, determination of the splanchnic oxygen consumption may be influenced by regional variations in the hepatic extraction of oxygen.

The calculations used for determination of mesenteric and hepatic arterial blood flow, mesenteric oxygen consumption, and hepatic arterial oxygen supply are interdependent, and errors involving one of these values may affect the others. The main assumptions are: *1*) the mesenteric oxygen consumption is unaffected by the clamping of the hepatic artery proper; *2*) hepatic venous blood flow during the clamping period equals the mesenteric blood flow in this period; *3*) blood obtained from the catheter in the portal vein is representative, as regards oxygen content, of mixed portal venous blood.

The first assumption cannot be tested without measurements of mesenteric blood flow by other methods. The second is probably not correct, since arterial blood may reach the liver by routes other than the hepatic artery proper (18, 19). Since this accessory hepatic arterial blood flow contributes to the hepatic venous blood flow, which during the clamping period is registered as mesenteric blood flow, the latter will be overestimated and the hepatic arterial blood flow and oxygen supply correspondingly underestimated. If the arterial anastomoses dilate immediately after the clamping of the hepatic artery proper, this error is exaggerated. Collateral flow between the portal bed and systemic veins does not influence the determination of the hepatic arterial blood flow unless it changes during the clamping period. It is not registered as mesenteric flow with the method used and is probably insignificant in patients without portal hypertension. If the interruption of the hepatic arterial flow is made proximal to the hepatic artery proper, the decrease in flow may be smaller, since many collaterals reach the hepatic artery at that level (20).

Determination of the oxygen content of portal blood may be erroneous for two reasons: the flow in the portal vein at the site of collection is probably laminar, and the portal blood may therefore not be homogenous as regards oxygen content. This error will influence the calculation of the mesenteric and hepatic oxygen consumption but, provided the error is the same during the control and the clamping periods, it will affect the calculated mesenteric blood flow only to a minor degree, since the error affects the numerator and the denominator of the equation similarly. The constancy of the mesenteric oxygen consumption during the clamping period in patients with two determinations (Table I) indicates that the difference between the portal oxygen content in the control and in the clamping period is not due to sampling error; in other words, the portal venous blood flow may change when the hepatic artery is clamped.

The chief limitation of the present method for the determination of hepatic arterial blood flow therefore lies in the assumption of a constant mesenteric oxygen consumption; its main potential error is that it disregards accessory arterial blood supply to the liver. For these reasons the values stated for arterial blood flow must be considered minimal values.

Hepatic arterial blood flow has been determined indirectly by Myers (21) in patients with cirrhosis of the liver, from whom portal blood could be obtained by puncturing dilated subcutaneous abdominal veins. In three patients it amounted to 25, 25, and 75 per cent of the hepatic blood flow. Apart from this study, determinations of the arterial blood flow to the human liver have

been confined to postmortem perfusion studies (22) which indicate that 30 per cent of the blood flow of the normal liver is derived from the artery.

In cats and dogs the hepatic arterial blood flow is between 15 and 40 per cent of the total liver blood flow, irrespective of the method used [mostly thermostromuhr or reduction in total flow after clamping the hepatic artery (1–4, 23–26)]. Our average figure for hepatic arterial blood flow is close to the upper limit of this range, but individual variations are very great, in the animal experiments as well as in our patients.

The fall in hepatic venous blood flow during the clamping period is on the average close to the calculated hepatic arterial blood flow, whereas the correlation between them is low ($r = +0.3$). This indicates that mesenteric blood flow (or accessory hepatic arterial blood flow, or both) in some cases increases and in others decreases when the hepatic artery proper is clamped; but on the average it decreases slightly, the oxygen consumption of the liver being maintained by means of the increased hepatic extraction of oxygen. In Patients 1 and 2 the oxygen tension of hepatic venous blood was reduced to less than 20 mm Hg. This indicates that hypoxic damage to the liver may be impending, but the fact that the serum transaminases did not rise in these cases is evidence against injurious tissue anoxia.

The mesenteric oxygen consumption amounts to about one-third of the total splanchnic oxygen consumption and therefore must be taken into account when the hepatic oxygen metabolism is studied by liver-vein catheterization. The value is greater than that assessed in the studies of Smythe, Fitzpatrick and Blakemore (27) and Bierman, White, Kelly and Steinbach (28), mainly because the arterioportal venous oxygen difference was greater in our patients.

The rise in the arterial concentration of BSP observed in most cases during the clamping period may be caused by reduced ability of the liver to eliminate the dye when hepatic arterial blood flow is cut off, but as the extraction percentage simultaneously rose from an average of 22 to an average of 28, it is more likely to be an effect of the reduced hepatic blood flow.

The average pressure in the femoral artery and the hepatic and portal veins remained constant, but in Patients 6 and 7 a definite rise in portal pressure occurred on clamping the hepatic artery and was followed by a decrease when the clamp was removed. Our results confirm that the transhepatic resistance is only a few per cent of the total splanchnic vascular resistance.

Conclusions. From the present studies it is concluded that the main function of the hepatic artery in man is to supply the liver with sufficient oxygen to compensate the relatively low oxygen content of the blood reaching it through the portal vein. Under the conditions studied, the oxygen requirements of the liver were apparently satisfied by the portal blood during the clamping of the hepatic artery, at the expense of a greater desaturation of the hepatic venous blood. If, however, under certain conditions the oxygen requirements of the liver rise, or the oxygen saturation of the portal venous blood falls owing to an increased mesenteric oxygen consumption [e.g., during absorption (27)] or to a decreased mesenteric blood flow [e.g., during shock (29)], the hepatic arterial blood supply may be essential for the normal functioning of the liver, since the mesenteric blood flow apparently does not rise to compensate the lack of oxygen in the liver.

Other functions of the hepatic artery have not been detected in this study. Hepatic arterial pressure seems to have no measurable influence on the normal portal venous pressure, in contrast to what is supposed by some authors to be the case in cirrhosis with portal hypertension (30, 31). Like Brauer, Shill and Krebs (32) we could not confirm the observation of Andrews, Maegraith and Richards (33) that the function of the hepatic artery is necessary for the elimination of BSP.

It is not possible from the present study to evaluate the late sequelae of ligation of the hepatic artery in man. The great individual variation in hepatic arterial blood flow found in our patients may, however, explain why the artery in some cases may be ligated without noticeable influence on the liver (34), while in other cases it is fatal (8). In the present short-term experiments the clamping of the hepatic artery in all cases seemed to be harmless.

SUMMARY

In eight patients the hepatic artery proper was clamped for an average of 24 minutes during

laparotomy. Hepatic arterial blood flow was calculated from hepatic venous blood flow (sulfobromophthalein method) and determination of hepatic and mesenteric oxygen consumption. This calculation implies a number of assumptions which are discussed in the text. The values of hepatic arterial blood flow given are presumably minimal, but apart from this the large scatter of the results may in part be due to methodological errors.

It was found that on an average: *1*) the hepatic arterial blood flow was 35 per cent (9 to 65 per cent) of the hepatic venous blood flow; *2*) the hepatic artery supplied 50 per cent of the hepatic oxygen consumption; *3*) the hepatic oxygen consumption was unchanged during the clamping; *4*) the extraction percentage of sulfobromophthalein increased, and there was no significant release of transaminases during the clamping (the liver function was therefore assumed to be unaffected); *5*) in two patients the portal pressure increased slightly; otherwise the portal and hepatic venous pressure remained constant during the clamping, and trans-hepatic and mesenteric resistance showed no significant change.

It is concluded that interruption of the hepatic arterial blood flow is initially compensated only by an increase of the portal-hepatic venous oxygen difference, and this seems to be sufficient to maintain normal liver function.

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