Effect of Portal Venous Blood Flow Diversion on Portal Pressure

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ABSTRACT To anticipate the hepatic vascular response to portacaval anastomosis, we studied portal pressure during diversion of portal blood through a temporary extracorporeal umbilical vein to saphenous vein shunt. The relationship of portal pressure to shunted flow was approximately linear. In five schistosomiasis patients (controls) portal diversion to 1,250 ml/min gave portal pressure-shunted flow curve slopes ranging from 0.13 to 0.57 cm water/100 ml per min (0.31±0.18, mean±SD). In 17 cirrhotic patients with portal hypertension a continuum of slopes was observed from within mean±2 SD of control (type A) to larger slopes (type B) indicating failure of portal pressure regulation. When portal flow was augmented by shunting from saphenous vein to portal vein, cirrhotic patients who had slopes less than mean±2 SD of controls during diversion (type A) exhibited a compliant system with small increases in portal pressure, whereas type B patients had significantly greater pressure increases. Selective investigations suggested that changes in portal pressure provoked compensatory changes in hepatic arterial blood flow that tended to maintain portal pressure at a set point. Type B patients demonstrated failure of this mechanism to varying degrees.

After end-to-side portacaval shunt, seven type A cirrhotic patients maintained residual intrahepatic venous pressure unchanged from prior portal pressure, whereas six type B patients had a significant decrease. Residual intrahepatic venous pressure was measured after portacaval shunt in 40 cirrhotic patients who were followed for as long as 9 yr (median survival 4.0 yr). The 13 patients who developed chronic encephalopathy had significantly lower pressure (21.1±4.4 cm, mean±SD) and shorter survival (median 0.6 yr) than the other 27 patients (32.6±5.3 cm, 5.0 yr). The preoperative estimation of portal pressure-diverted portal flow curve slope anticipates the hepatic vascular response to portacaval anastomosis and identifies a group of patients in whom loss of portal blood flow results in a low residual intrahepatic venous pressure that is associated with early death and chronic encephalopathy.

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INTRODUCTION

The increase in hepatic vascular resistance accompanying liver disease raises portal pressure and diminishes portal venous flow to the liver. Prograde portal flow may cease or even become retrograde as portal-systemic collaterals divert portal flow (1, 2). Increased hepatic arterial flow is presumed to compensate for reduced portal flow and account for normal values of total hepatic flow observed occasionally in cirrhotic patients with portal hypertension and portal systemic collateral circulation (3–6). An abrupt compensatory increase in hepatic arterial flow has been documented during acute portal flow diversion at the creation of a portacaval anastomosis (7–9). These facts imply homeostatic activity of the splanchnic vascular system to maintain portal pressure and/or hepatic blood flow when portal blood flow decreases (10–12). To evaluate the splanchnic hemodynamic response to portal blood flow diversion, we studied the response of portal pressure to acute incremental diversion of portal venous blood through a temporary extracorporeal umbilical vein to saphenous vein portal-systemic shunt (13).

METHODS

Subjects. In the schistosomiasis patients (Table I) described here, portal pressure and liver function tests including Bromsulfalein retention were normal. These patients were assumed to have normal splanchnic hemodynamics. They

were studied after heparinization, but before the administration of tartar emetic (13). The initial 17 cirrhotic patients (Table I) with documented esophageal varices were studied after umbilical vein catheterization for measurement of portal pressure (14), for umbilical vein angiography before portal-systemic shunt surgery (15), or for the establishment of an extracorporeal portal-systemic shunt to reduce portal pressure and control life threatening variceal hemorrhage (16). Subsequent patients evaluated before and after or during portacaval shunt received internal therapeutic end-to-side portacaval anastomosis after endoscopically documented variceal hemorrhage (17). In our institution umbilical vein catheterization is the preferred method for evaluating the portal circulation because of its safety and reliability (18). Informed consent was obtained from all subjects. These studies were performed under a research protocol approved by the Research Committee of the Veterans Administration Medical Center, New York, and the New York University School of Medicine.

Except where specifically indicated all procedures were performed under local anesthesia. The umbilical vein was catheterized extraperitoneally (19) and connected to a saphenous catheter by a silicon rubber tube with an occluding roller pump (solid state varistaltic pump; Manostat Corp., New York) and cannulating square wave electromagnetic flow meter (model E-3000; Statham Instruments Inc., Oxnard, Calif.). The umbilical vein catheter has an integral molded wire to prevent collapse and a second 1-mm lumen within its wall to allow continuous recording of portal pressure (model 1956 SP-BJBI, U. S. Catheter and Instrument Co., Glen Falls, N. Y.). Pressures were recorded using Statham P37 perfused strain gauges that permitted a continuous infusion of heparin (0.1 mg/min). Electrical mean pressures were used to obviate respiratory fluctuation. Zero pressure level was taken as 12 cm above the couch.

The hepatic vein was catheterized from an antecubital vein (20, 21). The achievement of a wedged position was confirmed by the demonstration of an arterial pulse in the pressure recording, by the identity of wedged hepatic venous pressure and portal pressure, and by injection of radiopaque contrast at the completion of a study.

Flow through the extracorporeal shunt was monitored by the cannulating square wave flow meter calibrated for zero flow with the shunt occluded. In vitro calibration for flow rates to 3,000 ml/min with pumped whole blood and occluding roller pump yields an accuracy of ±5%. The pumping circuit was primed with 200 ml of normal saline.

Procedure. After catheter placement and shunt construction, portal pressure was recorded and portal to systemic shunting initiated at 100 ml/min. Stabilization of pump rate required 5–10 s. By that time, pressures were stable and were recorded. Shunting was increased in 100 ml/min increments. When maximum hepatofugal flow was achieved as evidenced by portal vein flutter, shunting was stopped and pressure recorded. Systemic to portal shunting was then begun in 100 ml/min increments until limited by saphenous vein flutter. The shunting portion of the procedure required 15–20 min.

The response of portal pressure to shunting at different

TABLE I

Effect of Portal Venous Flow Diversion or Augmentation on Portal Pressure

Case	Diagnosis etiology	Documentation	Ascites (-4+)	Direction portal flow	Basal PP	Hepatofugal pumping			Hepatopetal pumping		
						Max flow	Pressure change	Pressure-flow slope	Max flow	Pressure change	Pressure-flow slope
					cm	*ml/min*	*cm*	*cm/100 ml*	*ml/min*	*cm*	*cm/100 ml*
1	C,A	Biopsy	0	Prograde	37	1,100	0	0.00	500	+2	+0.40
2	S	—	—	Prograde	15	750	−1	−0.13			
3	S	—	—	Prograde	11	1,200	−2	−0.17			
4	C,A	Biopsy	+1	Prograde	35	1,450	−3	−0.20			
5	S	—	—	Prograde	15	1,250	−3.5	−0.28			
6	C	Biopsy	3+	Prograde	27	1,600	−6	−0.38	1,000	+3	+0.30
7	S	—	—	Prograde	14	1,100	−5	−0.43			
8	C,A	Biopsy	0	Retrograde	37	900	−4	−0.44			
9	C,A	Biopsy	0	Prograde	36	1,000	−5	−0.50	700	+1	+0.14
10	S	—	—	Prograde	8	700	−4	−0.57	1,100	0	0.0
11	C,A	Biopsy	2+	Retrograde	39	1,700	−10	−0.59	1,200	+1	+0.08
12	C,A	W,biopsy	0	Prograde	35	2,500	−15	−0.60	900	+2.5	+0.27
13	C,HEM	Biopsy	+1	Prograde	29	1,500	−9	−0.60	600	+3	+0.50
14	C,A	Biopsy	0	Prograde	39	1,500	−13	−0.87	1,000	+16	+1.6
15	C,A	W,biopsy	2+	Prograde	42	600	−6	−1.00	1,400	+6	+0.43
16	C,A	Biopsy	1+	Prograde	26	1,000	−10	−1.00	750	+9	+1.20
17	C,CR	Biopsy	1+	Prograde	29	850	−18	−2.11			
18	C,A	Autopsy	0	Prograde	37	900	−28	−3.10	700	+11	+1.57
19	C,A	Biopsy	2+	Prograde	39	900	−31	−3.44	700	+9	+1.28
20	C,A	Biopsy	4+	Prograde	35	800	−31	−3.87			
21	C,A,HEP	Biopsy	0	Prograde	55	1,100	−48	−4.36			
22	C,A	Biopsy	0	Prograde	35	500	−30	−6.00	500	+18	+3.6

Abbreviations used in this table: C, cirrhosis; S, schistosomiasis; A, alcoholism; HEM, hemachromatosis; HEP, hepatoma; CR, cryptogenic; W, wedged hepatic venous pressure; PP, portal pressure; max, maximum.

vascular volumes was studied after phlebotomy accomplished by draining the extracorporeal circuit into a sterile infusion bottle containing 20 mg of heparin. 1 liter of blood was withdrawn in 3 min. After studying the response of portal pressure to shunting the blood was reinfused. Then, for volume expansion 5% dextran or blood was infused. Final volume was dictated by the patient's clinical status (22). Since the elapsed time for phlebotomy and volume expansion was <15 min, vascular volume shifts were considered to be negligible. Therefore, changes in blood volume were calculated from the measured quantity withdrawn or infused.

At the completion of a study the direction of portal venous flow (prograde or retrograde) was determined by observing the course of a gentle hand injection of 50% sodium diazotrate (Hypaque, Winthrop Laboratories, Sterling Drug Co., New York) through the primary lumen of the umbilical vein catheter (3). Radiopaque contrast media were not administered before pressure or flow measurements because of their effect on systemic and splanchnic hemodynamics (23). Finally, a pressure injection with serial x rays was used to visualize the portal vasculature (15).

Definition of residual intrahepatic venous pressure. Wedged hepatic venous pressure and portal pressure measured by umbilical vein catheterization are identical in patients with cirrhosis when the portal circulation is intact (24). Simultaneous measurement of wedged hepatic venous pressure and umbilical portal pressure in two cirrhotic patients during shunting of portal flow agreed within ±1 cm water (Fig. 1). After disconnection of the extrahepatic portal venous system from the liver by end-to-side portacaval shunt, residual intrahepatic venous pressure was measured by wedged hepatic venous catheterization or by umbilical vein catheterization of the intrahepatic portal vein. The extrahepatic portal venous system drains into the vena cava.

Construction of portal pressure-shunted portal flow curves. Curves constructed for controls with *Schistosoma mansoni* infections and cirrhotic patients with portal pressure-shunted portal flow curve slopes < −0.67 cm water/100 ml per min diverted flow were linear (Figs. 1 and 2) and allow a simple arithmetic expression of slope as change in pressure/100 ml per min shunted flow. Cirrhotic patients with steep slopes have a smaller range of flow and curves that are increasingly convex (Figs. 2 and 3). For the purpose of this paper, the arithmetic portal pressure-shunted portal flow curve slope is derived from the sum change in pressure divided by maximum flow before vein flutter was detected by palpation of the shunt or pumping was stopped because of increased portal pressure. As indicated, certain patients were studied at laparotomy under anesthesia or during rescuscitation from hemorrhage. These circumstances provide unique opportunities to gain physiologic insights in man but undoubtedly influence to a greater or lesser extent the data obtained. Therefore, we confined data in Table I describing the control (schistosomiasis) patients and values in cirrhotic patients with portal hypertension for portal pressure-shunted portal flow curve slope to subjects studied without anesthesia or laparotomy when hemodynamically stable.

Statistical significance was determined with the Wilcoxon two sample ranked test, unpaired *t* test, and log rank test (25, 26).

RESULTS

Schistosomiasis (control) subjects

During portal to systemic shunting averaging 1,000 ml/min (range, 700–1,350) in five schistosomiasis pa-

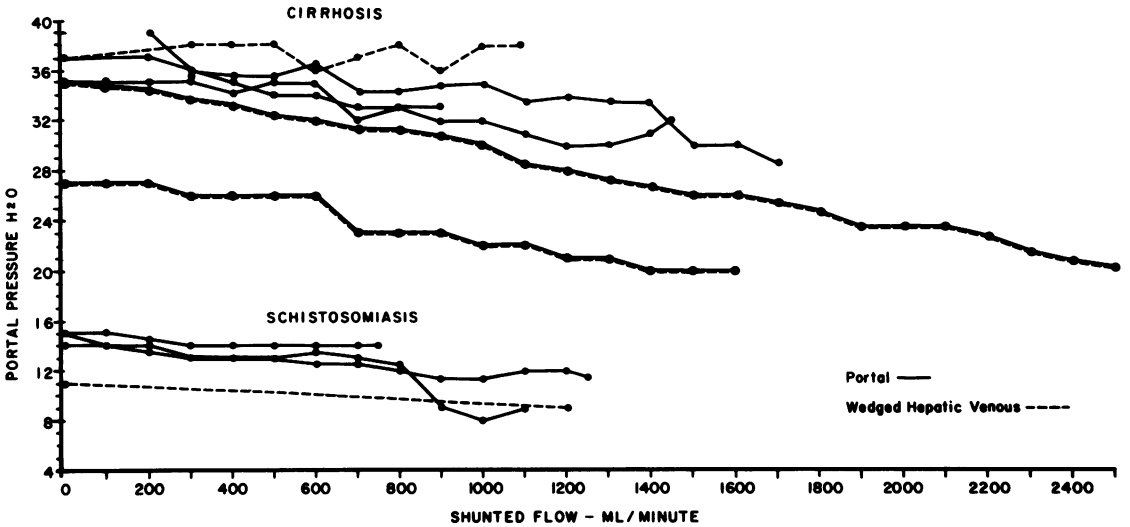

FIGURE 1 Response of portal pressure to portal venous blood flow diversion in type A cirrhotic patients and control subjects. Portal pressure (centimeters water) is plotted against volume of shunted portal venous flow (milliliters per minute) diverted through an umbilicosaphenous shunt. Six representative cirrhotic patients are shown in order of decreasing basal portal pressure (case Nos. 11, 1, 8, 4, 12, and 6, Table I). Four representative controls (2, 5, 7, and 3, Table I) are shown in order of decreasing basal portal pressure. The solid line indicates portal pressure measured through an umbilical vein catheter in the left portal vein. The interrupted line indicates portal pressure measured by wedged hepatic venous catheterization. The combined solid and interrupted lines in two cirrhotic patients (11, 1, Table I) indicate simultaneous measurement of portal and wedged hepatic venous pressures.

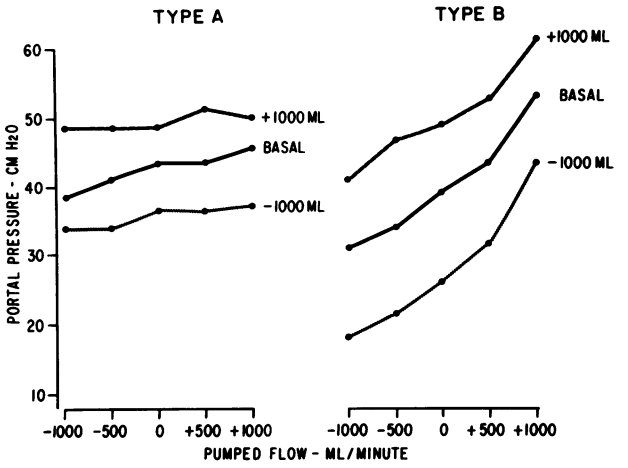

FIGURE 2 Effect of changes in blood volume on portal pressure and portal pressure-shunted flow curve slope. In a single type A patient (left) basal portal pressure of 43 cm was reduced to 36 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000 ml-volume load in addition to replacement of the 1,000-ml phlebotomy, whereas portal pressure-shunted flow slope varied from 0.35 to 0.15 to 0.10 cm/100 ml per min shunted flow, respectively. In a single type B patient, a basal portal pressure of 39 cm was reduced to 26 cm by a 1,000-ml phlebotomy and increased to 48 cm by a 1,000-ml volume load after replacement of the phlebotomy, whereas portal pressure-shunted flow curve slope varied from 1.15 to 1.25 to 1.05, respectively.

tients portal pressure decreased an average of 3.1 cm water (range, 1–4). Portal pressure-shunted portal flow slope averaged -0.31 ± 0.18 (mean±SD) cm water/100 ml per min diverted flow (range -0.13 to -0.57) (Table I).

Cirrhotic patients

In cirrhotic patients (n = 17) with portal hypertension, the response to portal diversion was varied and the portal pressure-shunted portal flow slope ranged from -0.0 to -6.0. In patient 1 (Table I) portal pressure was unchanged by portal diversion of 1,000 ml/min, whereas in patient 22 (Table I) portal pressure fell to central venous levels with diversion of only 500 ml/min (Table I). A histogram (Fig. 4, upper) of portal pressure-shunted portal flow slope during diversion in cirrhotic patients with portal hypertension shows a continuum from slopes similar to *S. mansoni* patients with normal portal pressure (Fig. 4, hatched bars) to extremely high values. A relationship between basal portal pressure and portal pressure-shunted portal flow slope is not apparent (Table I). The lack of correlation between portal pressure and portal pressure-shunted portal flow slope arises, in part, from the influence of blood volume on portal pressure (Fig. 2). Increasing or decreasing blood volume produces a corresponding shift in portal pressure (22) with little change in portal pressure-shunted portal flow slope.

Definition of type A and B cirrhotic patients

Type A cirrhotic patients (Figs. 1 and 2) are defined as those with portal pressure-shunted portal flow slopes < -0.67 cm/100 ml per min (control mean±2 SD). Type B cirrhotic patients have portal pressure-shunted portal flow slopes in excess of -0.67 cm/100 ml per min diverted flow (Table I, Figs. 2 and 3). In the initial 17 patients studied (Table I) the mean basal portal pressure (34.4±4.2 cm of water, mean±SD) of eight cirrhotic patients with portal pressure-shunted flow slopes for portal flow diversion within the mean±2 SD of the five control (schistosomiasis) patients was not significantly different from the mean basal portal pressure (37.4±8.3 cm) of the nine cirrhotic patients with greater slopes. Similarly, in a group of 13 patients clinically considered candidates for portacaval anastomosis (Fig. 5), the basal portal pressures of seven type A patients were not significantly different from the six type B patients. The 23 cirrhotic patients with endoscopically documented bleeding esophageal varices classified as type A or type B when hemodynamically stable under local anesthesia had basal portal pressure ranging from 55 to 26 cm. The 55-cm value (Table I, No. 21) occurred in a patient with hepatoma. Although the three highest values (55, 45, and 42 cm) and the two lowest values (26 and 28 cm) were found in type B patients, the pressures of type A patients were not significantly different (Wilcoxon rank test) from type B.

Mechanism for maintenance of portal pressure during portal venous flow diversion

Hepatic arterial response to extracroporeal portal diversion. Hepatic arterial flow was measured at laparotomy for portacaval anastomosis by noncannulating square wave electromagnetic flow meter in two type A cirrhotic patients before and during diversion of 1 liter/min. Hepatic arterial flow increased 40 and 46%.

Spontaneous total retrograde portal flow in type A portal hypertension. Two (Nos. 8 and 11) of 17 cirrhotic patients described had total retrograde portal venous flow (Table I) (3). Both had type A portal hypertension with portal pressure-shunted portal flow slopes of 0.44 and 0.59 cm/100 ml per min. The presence of total retrograde portal flow implies sufficient portal-systemic collateral vessels for egress from the splanchnic chamber of all splenic and mesenteric inflow and a portion of hepatic arterial flow. The most likely source for additional splanchnic inflow to maintain portal pressure during portal diversion in this situation is the hepatic artery.

Portal pressure response to portal flow augmentation by systemic to portal shunting. In portal hypertension an added load should increase portal pressure, since mechanisms for reducing splanchnic inflow or in-

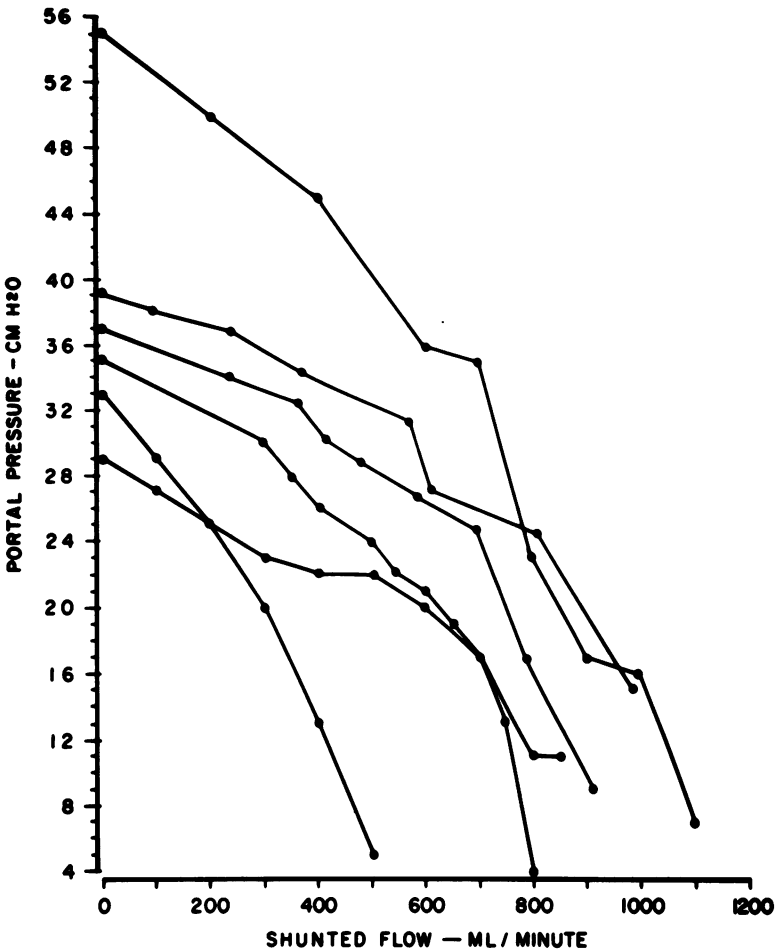

FIGURE 3 Response of portal pressure to portal diversion in type B cirrhotic patients. Portal pressure (centimeters water) is plotted against volume of portal venous flow diverted through the umbilicosaphenous shunt. Six representative type B cases in order of decreasing basal portal pressure (case Nos. 21, 19, 18, 20, 22, and 17, Table I) are shown.

creasing outflow already would be activated by existing portal hypertension. Type A patients accommodate their portal pressure as well to portal flow augmentation as diversion (Table I, Figs. 2 and 4). Portal pressure-shunted portal flow curve slopes are more varied for augmentation but are similar to slopes (Table I) for diversion in the 12 patients where both maneuvers were performed (Fig. 4).

Type A cirrhotic subjects who during portal diversion had portal pressure-shunted portal flow slopes less than the mean±2 SD of control exhibit a compliant system in that relatively small increases in portal pressure were observed (range, +0.08 to +0.50, mean±SD, 0.3±1.6 cm/100 ml per min, $n = 6$). Cirrhotic patients with steep type B slopes during portal diversion demonstrated steep slopes during augmentation (range, +0.43 to +3.60, mean±SD, 1.6±1.1 cm/100 ml per min, $n = 6$) that were increased ($P < 0.01$) when compared to the compliant group. The basal portal pressures of the eight cirrhotic patients with type A slopes (34.4±4.2 cm water, mean±SD) were not significantly different from the nine cirrhotic patients with type B slopes (37.4 ±8.3 cm water).

Induced retrograde portal flow during portal venous flow diversion. If increasing hepatic arterial flow, rather than changing portal-systemic collateral, splenic, or mesenteric inflow, accounts for the maintenance of portal pressure during portal diversion, sampling of indocyanine green from the umbilicosaphenous shunt during diversion should demonstrate extraction of indocyanine green from portal blood when increased hepatic arterial flow reverses through hepatic sinusoids to enter the extracorporeal circuit. At laparotomy for portacaval shunt with 750 ml/min portal diversion, prograde portal flow was evidenced by absence of extraction. Retrograde flow of hepatic arterial blood into the

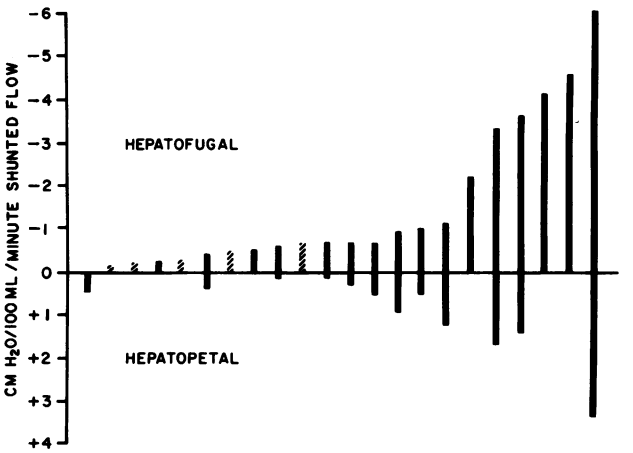

FIGURE 4 Histogram of portal pressure-shunted portal venous flow slope. Patients 1 (left) through 22 (right) are presented in order of increasing slope (Table I). The upper bars refer to the slope for portal diversion (hepatofugal shunting). The lower bars refer to the slope for portal blood flow augmentation (hepatopetal shunting) performed in 12 patients. Hatched bars indicate schistosomiasis patients (controls).

portal vein with extraction occurred at diversion rates in excess of 1,000 ml/min. This type A patient (Table IIA) accommodated to 1,000 ml/min portal diversion or augmentation (portal pressure-shunted portal flow slope −0.3, +0.0) with little change in portal pressure.

Portal pressure and intrahepatic venous pressure response to occlusion of hepatic artery or portal vein. Intraoperative occlusion of hepatic artery or portal vein before and during diversion of blood from the hepatic side of the occluded portal vein was studied in two patients to compare hepatic artery and portal venous (splenic and mesenteric) capacity to sustain intrahepatic venous pressure (Table II). Intrahepatic venous pressure was measured and blood was shunted through the umbilical catheter on the hepatic side of the occluded portal vein.

The type A patient maintained intrahepatic venous pressure with flow from either hepatic artery or portal vein (Table II experiments 5A and 6A). Portal venous flow alone maintained portal venous pressure when the hepatic artery was occluded (experiment 5A) suggesting adequate portal flow to support pressure. When portal flow is stopped, hepatic artery flow is adequate to prevent a reduction in intrahepatic venous pressure (experiment 6A). The response to 1,000 ml/min portal to systemic shunting between the site of portal vein occlusion and the liver (experiment 7A) shows the hepatic artery to have a greater capacity to support intrahepatic venous pressure than mesenteric and splenic vessels, since pressure falls less when the portal vein is occluded and the hepatic artery supplies the liver (experiment 8A) than when the hepatic artery is occluded and the portal vein supplies liver (experiment 7A). This suggests that increased hepatic artery flow is the most important mechanism in maintaining portal pressure during portal diversion in this type A patient.

In a type B patient (Table II) occlusion of the portal vein precipitated an 11-cm decrease in intrahepatic venous pressure (experiment 6B) indicating the failure of hepatic artery flow to maintain pressure. This inadequacy was exaggerated by simultaneous portal vein occlusion and portal diversion (Experiment 8B). This type B patient relies on portal flow to sustain intrahepatic venous pressure. The failure of hepatic artery occlusion to reduce portal pressure (experiment 5B) indicates a small hepatic artery contribution to maintenance of portal pressure in this patient. The steep portal pressure-shunted portal flow slope when the portal vein is patent (experiment 2B) demonstrates the failure of portal-systemic collateral flow to compensate for increasing or decreasing portal flow.

Maintenance of residual intrahepatic venous pressure after end-to-side portacaval anastomosis. If the portal pressure-shunted portal flow slope estimates he-

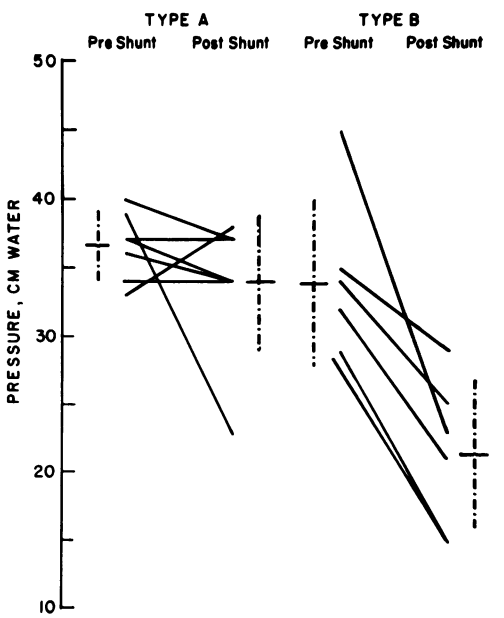

FIGURE 5 Effect of total portal venous flow diversion by end-to-side portacaval anastomosis on intrahepatic venous pressure in type A and type B patients. The horizontal solid bar indicates the mean. The vertical interrupted line indicates SD. Preoperative portal pressures for type A and type B patients were not significantly different. After portacaval shunt mean intrahepatic venous pressure in type B patients (21.3±5.6, $n = 6$) is significantly decreased ($P < 0.01$) when compared to preshunt portal pressure or postshunt intrahepatic venous pressure in type A patients (33.9±5.0, $n = 7$). Four type A and four type B patients shown here had portal pressure-shunted portal flow slope determined under anesthesia at laparotomy for portacaval anastomosis and are excluded from Table I.

TABLE II

Response of Intrahepatic Venous Pressure to Occlusion of Hepatic Artery and Portal Vein

Experiment	Hemodynamic type	A	B
1	Basal portal pressure	46	29
2	Portal pressure during diversion, 1,000 ml/min	43	16
3	Portal pressure during augmentation, 1,000 ml/min	46	37
4	Pressure-flow slope (cm water/100 ml per min)		
	diversion	−0.3	−1.3
	augmentation	+0.0	+0.8
5	Portal pressure with hepatic artery occluded	44	31
6	Intrahepatic pressure with portal vein occluded	44	18
7	Portal pressure with hepatic artery occluded plus diversion, 1,000 ml/min	35	22
8	Intrahepatic pressure portal vein occluded plus diversion, 1,000 ml/min	39	3

patic vascular capacity to sustain portal pressure during portal venous diversion, the residual intrahepatic venous pressure after end-to-side portacaval anastomosis when the hepatic artery alone supplies the liver should correlate with the preoperative portal pressure and postoperative intrahepatic venous pressure. In 13 patients undergoing end-to-side portacaval anastomosis (Fig. 5) after determination of portal pressure-shunted portal flow slope preoperative portal pressure in seven type A patients (36.6±2.5 cm, mean±SD) was not significantly different from six type B patients (33.8±6.1 cm). After end-to-side portacaval anastomosis in type A patients intrahepatic venous pressure was not significantly changed (33.9±5.0) indicating hepatic vascular compensation for loss of portal venous flow. Type B patients suffered a decrease in intrahepatic venous pressure (21.3±5.6) that was significant when compared to their preoperative portal pressure ($t = 3.38$, $P < 0.01$) or to the postoperative intrahepatic venous pressure of the type A patients ($t = 3.90$, $P < 0.01$).

Residual intrahepatic venous pressure after end-to-side portacaval shunt and prognosis. Our initial clinical observations suggested that type B patients in whom residual intrahepatic venous pressure fell after portacaval anastomosis (Fig. 5) frequently died shortly after surgery or suffered from chronic encephalopathy. Therefore, residual intrahepatic venous pressure was measured in 40 patients with cirrhosis associated with ethanol abuse shortly after interval end-to-side portacaval anastomosis when they were hemodynamically stable. The patients were followed clinically for as long as 9 yr (median, 4.0 yr). 13 patients developed chronic hepatic encephalopathy defined as diminished mental function that was improved by and required continued dietary protein restriction and antibiotic or lactulose therapy. Six of these died within 1 mo of surgery and were classified as early deaths (Fig. 6). The mean residual intrahepatic venous pressure of these 13 patients (21.1±4.4 cm) was significantly less ($P < 0.001$) than the 27 patients that did not have chronic encephalopathy (32.6±5.3 cm).

Life table analysis (25, 26) demonstrated a significantly ($P < 0.01$) shorter survival (median, 0.6 yr) for the 13 patients with lower pressures when compared to the other patients (median, 5.0 yr) (Fig. 7). None of the 27 patients with relatively favorable postoperative courses had a residual intrahepatic venous pressure <25 cm. 6 of 8 patients who died within 1 mo, 8 of 10 patients who died within 1 yr, and 6 of 7 patients who survived the postoperative period, but suffered from chronic encephalopathy, were unable to maintain residual intrahepatic venous pressure above 25 cm. These findings suggest that 25 cm is a critical lower limit of pressure, below which hepatic function is not maintained and chronic encephalopathy with early death supervenes.

DISCUSSION

A lesser fall in portal pressure than would be expected for a given quantity of portal blood flow diversion indicates a compensatory vascular mechanism. Therefore, the steepest portal pressure-shunted portal flow slope observed (Table I, patient 22) most clearly approaches the absence of this postulated mechanism. Lesser slopes result from its activity. The failure of the portal pressure-shunted portal flow slope to be altered by changing blood volume, portal pressure, and presumably cardiac output (27) points to a splanchnic rather than systemic origin of the proposed mechanism. The small portal pressure-shunted portal flow slopes recorded in control subjects may reflect both low and variable hepatic resistance to flow (28, 29). Similarly, a lesser increase in portal pressure than expected during portal blood flow augmentation by systemic to portal shunting in the presence of portal hypertension suggests a compensatory decrease in arterial inflow to the splanchnic chamber since hepatic and portal-systemic collateral outflow resistance should be limiting when cirrhosis and portal hypertension are present (30–32). Failure or absence of this mechanism in some patients with cirrhosis is indicated by the continuum of portal pressure-shunted portal flow slopes observed.

An increase of mesenteric and splenic venous flow

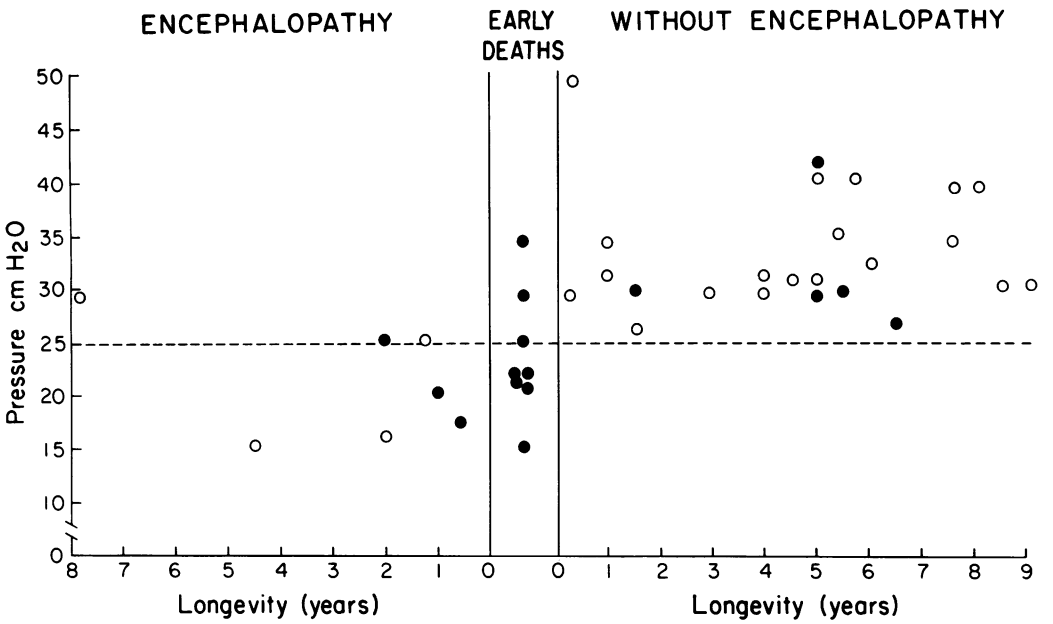

FIGURE 6 Relationship of survival and clinical status (encephalopathy) to residual intrahepatic venous pressure after end-to-side portacaval anastomosis (open circle, alive; closed circle, dead). The 13 patients with encephalopathy (left) had significantly lower pressures than those without encephalopathy (right, $n = 27$) and a significantly shorter survival (median, 0.6 vs. 5.0 yr). Early mortality is defined as death within 1 mo of surgery.

in response to reduced portal pressure is suggested by the maintenance of portal pressure despite hepatic artery occlusion (Table II) and published studies demonstrating an increase in portal and splenic flow after portacaval anastomosis (10, 33). Hepatic (9, 34–36), mesenteric, and splenic (33) arteries may all contribute to maintenance of portal pressure in type A patients when the portal circulation is intact. Conversely, the steep portal pressure-shunted portal flow slopes in type B patients indicate a limited response of all these vessels to changing portal flow and suggests a widespread defect in vascular function.

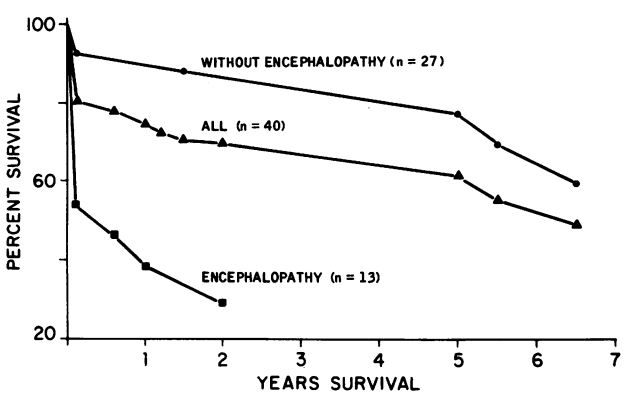

FIGURE 7 Life table analysis of 40 patients followed for up to 9 yr after end-to-side portacaval anastomosis (center curve, all patients). The 13 patients with chronic encephalopathy had a lower residual intrahepatic venous pressure and reduce median survival (0.6 yr, lower curve) when compared to the 27 patients with residual intrahepatic venous pressure > 25 cm and medial survival 5.0 yr who did not have chronic encephalopathy (highest curve). The highest and lowest curves are significantly different (log rank test, $P = 0.01$). Cumulative survival for the 13 patients in the lower curve was not carried beyond 2 yr because experience was limited to only two patients surviving beyond this point.

Abnormal vascular responses in the cardiac (37, 38), pulmonary (39), renal (40), integumentary (41), and splanchnic (36) systems have been demonstrated in patients with liver disease. The increased cardiac output (37) functional renal failure (42) and portal hypertension (43) of liver disease may be reversible. The portal hypertension of cirrhotic patients in this study consisting of an elevated portal pressure setpoint and a variable limitation of the response to changing portal flow also, at least in part, may be a reversible alteration in vascular responsiveness (44) rather than a consequence of the presumed fixed anatomic hepatic outflow block previously conceived as the cause of portal hypertension (45).

Alternatively, the continuum of response to changing portal flow could result from anatomic alterations in the hepatic artery associated with cirrhosis (46, 47). Herrick (48), and later Dock (49), perfused the livers of alcoholic hypertropic cirrhotic patients in vitro and demonstrated a reciprocal relationship between hepatic arterial pressure and portal pressure. They speculated on the role

of relatively increased hepatic arterial flow as a factor in the portal hypertension of cirrhosis associated with alcoholism. The investigations reported here were based upon their early studies and imply similar conclusions.

Moreno et al. (1) and Burchell et al. (9) have studied portal and hepatic arterial blood flow at laparotomy for portacaval anastomosis. They demonstrated an elevated setpoint for portal pressure of 40 cm of water since this pressure was found despite wide variation in portal blood flow (10). Attempts to correlate portal or hepatic arterial flow measured before or immediately after portacaval anastomosis with prognosis failed (9).

After our initial publications, Reynolds (50) attempted and failed to correlate wedge hepatic venous pressure measured after portacaval shunt with prognosis. His data were drawn retrospectively from studies of hepatic blood flow after portacaval shunt (51, 52) and, therefore, excluded patients who died early or had poor liver function that precluded blood flow measurement. Furthermore, the additional variable of inferior vena caval pressure was introduced by subtracting inferior vena caval pressure from the wedged hepatic venous pressure. Subsequently, Burchell et al. (53) retrospectively correlated a limited increment in hepatic arterial flow occurring after portacaval shunt with early death and encephalopathy. Patients with less than a 200 ml/min increase in hepatic arterial flow after diversion of portal flow by portacaval shunt accounted for 90% of the patients with encephalopathy or early mortality. Unfortunately, their hemodynamic data did not include residual intrahepatic venous pressure. Nevertheless, their retrospective analysis of intraoperative data and correlation of hemodynamic response to long-term prognosis confirms the data presented here.

The prolonged survival and absence of hepatic encephalopathy in patients with residual intrahepatic pressures >25 cm suggests that this is the minimum pressure required to sustain hepatic function. The elevated portal pressure set point of 40 cm, maintained in these patients before portacaval shunt when they were at risk for variceal hemorrhage, is on the average 15 cm greater. This 15-cm excess of portal pressure appears to increase the risk of variceal hemorrhage without serving an essential role in maintaining hepatic perfusion.

There is general agreement that prior hemodynamic measurements have been of "inconsistent value in selecting the proper shunt to be done or in predicting its physiologic outcome" (54). The preoperative hemodynamic classification presented here allows a prospective quantitative stratification of cirrhotic patients that identifies the type B patients who require portal blood flow to maintain hepatic perfusion and the type A patients who tolerate the loss of portal flow produced by portacaval anastomosis relatively well.

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