Bleeding from esophageal varices in cirrhosis of the liver:

Hemodynamic and radiological criteria for the selection of potential bleeders through hepatic and umbilicoportal catheterization studies

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Summary: Combined hepatic and umbilicoportal catheterization was performed in 38 compensated cirrhotics. Portohepatography with opacification of the coronary vein was obtained in all cases. The free portal venous pressure (FPVP) and the wedged (WHVP) and free (FHVP) hepatic venous pressures were recorded. The portohepatic gradient (FPVP-FHVP) was used as an index of portal hypertension. The coronary vein was separately re-evaluated for varices and graded as 1+ to 4+.

Eighteen patients had varices graded as 3+ or 4+ (Group A) and all had a portohepatic gradient of 10 mm. Hg or more. The other 20 cirrhotics (Group B) had varices graded as 1+ or 2+ and 15 had a portohepatic gradient of less than 10 mm. Hg. The difference between gradients of Group A and Group B was highly significant.

Of the 38 cirrhotics studied, eight had bled from varices and all are included in Group A. There is no significant difference between the gradients of both bleeders and non-bleeders of Group A.

There is a significant correlation between the presence of large varices with a portohepatic gradient of 10 mm. Hg or more and a high risk of variceal bleeding. The radiological and hemodynamic data obtained by combined hepatic and umbilicoportal catheterization in cirrhosis of the liver can be of significant help in the selection of potential bleeders.

Bleeding from esophageal varices is a major cause of death in cirrhosis of the liver, and for more than 20 years therapeutic portocaval and splenorenal shunts have been performed as management of this complication. This approach has reduced the risks of bleeding from esophageal varices in patients who survived both the initial hemorrhage and the operation.

In view of the high mortality related to variceal bleeding, prophylactic portocaval shunt was then suggested. Controlled studies performed by different groups[1-3] have failed to show any improvement in long-term survival rate. Recently, Conn and Lindenmuth[2] described a subgroup of cirrhotics, those with overt ascites, in whom it was believed that prophylactic portocaval shunt might prove beneficial. A further study by Conn,[4] where cirrhotic patients with ascites and esophageal varices were included in a controlled prospective evaluation of prophylactic portocaval shunt, has shown, after four years, a longer survival rate in the patients who were subjected to a shunt operation than in the controls.

During a general investigation of cirrhotics with portal hypertension, using combined hepatic and umbilicoportal catheterization,[5, 6] our group has been interested in the radiological and hemodynamic characteristics of the cirrhotic patients with variceal bleeding. The present report deals with the results obtained in 38 cirrhotics, eight of whom have bled from esophageal varices.

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TABLE I

Pertinent clinical and laboratory data on the 38 cirrhotic patients

Case no.	Sex	Age	Bilirubin (mg. per 100 ml.) Total	Bilirubin (mg. per 100 ml.) Conjugated	Transaminases SGO	Transaminases SGP	Alkaline phosphatase (Bodansky units)	BSP 45 min.	Cholesterol (mg. per 100 ml.)	Proteins (g. per 100 ml.) Alb.	Proteins (g. per 100 ml.) G.-G.	Bleeding Liver biopsy	Bleeding from varices	Ascites*	Alcohol
1	M	56	1.05	0.45	52	44	1.84	4.25	90	3.67	3.33	+	—	—	+
2	M	41	0.10	0.07	90	30	2.24	7.25	200	4.21	1.34	+	—	—	+
3	M	50	0.45	0.22	99	30	2.75	10.0	150	3.67	2.21	+	+	—	—
4	M	55	0.5	0.15	82	35	1.93	12.75	220	2.82	1.11	+	—	—	+
5	F	47	1.35	0.5	89	59	3.29	11.6	185	3.24	1.56	+	—	—	—
6	M	38	3.35	1.7	84	34	5.08	18.6	143	4.12	3.83	+	+	—	+
7	M	57	2.82	1.7	96	48	3.7	—	118	2.45	3.60	+	—	+	+
8	M	45	0.9	0.5	71	34	2.9	27.5	150	3.24	1.82	+	+	+	+
9	M	48	3.3	1.7	110	80	4.1	29.0	270	2.81	2.21	+	—	—	+
10	M	48	0.8	0.25	28	21	2.84	23.7	96	3.56	1.23	+	+	+	+
11	M	47	1.45	0.82	30	34	3.11	18.6	67	3.36	1.28	+	+	+	+
12	M	34	0.55	0.35	132	64	1.91	16.0	153	4.56	2.31	+	—	—	+
13	M	37	0.3	0.1	50	47	4.25	11.6	153	4.42	1.45	+	—	—	+
14	M	43	2.75	1.37	118	55	2.27	—	165	2.68	1.45	+	—	+	+
15	M	52	0.58	0.47	84	36	1.73	14.0	204	4.46	1.81	+	—	+	+
16	M	29	1.5	1.0	79	20	2.08	—	148	2.58	1.89	+	—	+	+
17	M	67	1.8	0.95	63	15	4.67	22.75	—	2.85	2.04	+	—	+	+
18	M	40	0.3	0.15	47	58	2.2	3.37	183	4.07	2.04	+	—	—	+
19	M	55	0.3	0.2	22	14	0.42	3.0	170	2.64	1.98	+	—	—	+
20	M	33	0.4	0.27	42	11	2.17	—	168	3.94	2.42	+	—	—	+
21	F	49	1.1	0.3	30	17	3.25	10.0	127	3.57	2.29	+	—	—	+
22	F	35	0.05	0.03	70	54	1.42	7.5	178	4.11	1.44	+	—	—	+
23	F	39	2.3	1.25	58	19	2.92	21.08	198	3.57	2.16	+	+	+	+
24	M	44	1.15	0.42	70	31	2.14	15.3	192	3.65	1.66	+	—	—	+
25	M	38	0.7	0.2	44	35	3.7	—	147	3.96	2.80	+	—	—	+
26	M	59	2.4	1.77	66	60	3.7	24.75	96	2.54	1.63	+	—	+	+
27	M	48	3.4	2.4	222	62	6.99	37.25	222	2.78	1.26	+	—	+	+
28	M	49	0.95	0.32	186	78	2.53	22.5	270	5.33	1.30	+	—	—	+
29	M	36	3.05	1.4	48	18	2.4	—	129	3.58	2.94	+	+	+	+
30	F	41	0.45	0.15	49	25	3.77	—	171	4.66	1.88	+	—	—	+
31	M	37	0.85	0.8	35	30	3.3	—	197	3.95	0.97	+	—	—	+
32	M	54	2.02	1.01	62	12	4.1	—	229	3.57	2.21	+	+	+	+
33	M	58	0.9	0.32	30	7	4.0	—	61	3.65	2.38	+	—	+	+
34	M	42	0.6	0.5	108	25	4.66	15.0	200	4.01	1.90	+	—	—	+
35	M	57	0.4	0.02	26	25	2.36	6.75	123	4.78	1.1	+	—	—	+
36	M	37	0.3	0.12	17	19	1.68	10.25	189	4.26	1.59	+	—	—	+
37	M	66	0.80	0.45	35	15	2.59	2.8	131	3.42	1.22	+	—	+	+
38	M	48	0.06	0.035	18	42	2.19	—	285	3.81	1.22	+	—	—	+

*Known history of ascites before bleeding or before procedure was performed.

Material and methods

Thirty-eight compensated cirrhotics, 34 males and four females aged 29 to 67 years (mean: 46.3 years), were submitted to combined umbilicoportal and hepatic vein catheterization. Pertinent clinical and laboratory findings are shown in Table I. All were alcoholics but two (Cases 3 and 5), one of whom (Case 3) had variceal bleeding. At the time of the study, none of the patients had ascites or clinical jaundice.

Diagnosis of cirrhosis was confirmed by needle biopsy of the liver in all patients. Upper gastrointestinal radiological studies were obtained in all cases but esophagoscopy was not performed. Eight patients bled from esophageal varices (Table I) and a portocaval shunt was performed in six of these (Cases 3, 6, 8, 10, 11 and 29). Two bleeders had never had ascites before their bleeding episode (Cases 3 and 6).

Umbilicoportal catheterization was carried out according to a technique described elsewhere.[7] Portohepatography was obtained by injecting 50 ml. of meglumine diatrizoate (Renografin 76, Squibb) at a pressure of 60 lbs. per square inch. Sixteen radiographs were then taken using a rapid film changer as follows: two per second for three seconds, one per second for eight seconds and one at 20 and at 40 seconds. The coronary vein (CV) was opacified in all cases, and its involvement was separately evaluated and graded as 1+ to 4+ (Figs. 1 to 5). Other collaterals contributing to the formation of gastroesophageal varices, as shown by retrograde splenography (Fig. 6), were not taken into account in the present study, since this procedure was not carried out in all cases.

Using a method described by others,[8, 9] hepatic vein catheterization was performed and pressures were recorded in both the wedged (WHVP) and the free (FHVP) positions. Free portal venous pressure (FPVP) was also recorded. WHVP and FPVP were recorded within a period of two minutes using the same transducer and electronic manometer. Each pressure reading was recorded on at least two occasions and for each an electronic mean was obtained. The portohepatic gradient was determined by subtracting the FHVP value from the FPVP value and was used as an index of portal hypertension.[6]

Results

Results are listed in Table II. Eighteen subjects had varices graded as 3+ or 4+ and formed Group A (Fig. 7 and Table III).

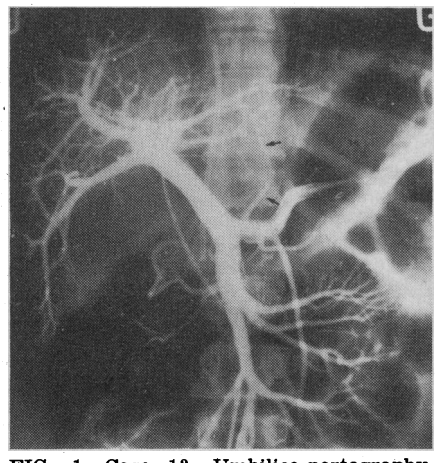

FIG. 1—Case 13. Umbilico-portography (one second). Normal coronary vein without inverted circulation graded as 1+ (arrows). Good opacification of the superior and inferior mesenteric veins. (There is a catheter in the inferior vena cava.)

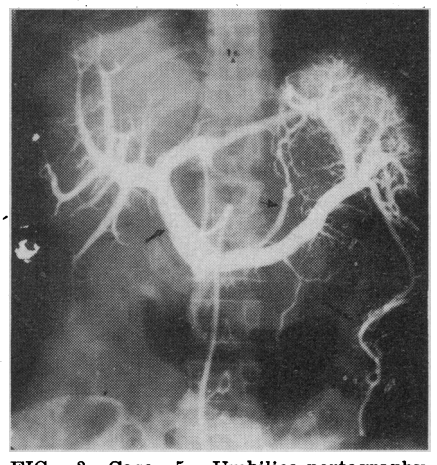

FIG. 2—Case 5. Umbilico-portography (one second). Minimally dilated and tortuous coronary vein without inverted circulation graded as 1+ (upper arrow). There is good opacification of the splenic vein with retrograde splenography.

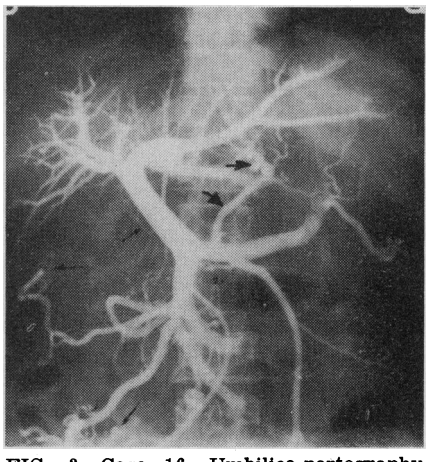

FIG. 3—Case 16. Umbilico-portography (two seconds). Slightly dilated and tortuous coronary vein with inverted circulation (upper arrows). Minimal esophageal varices graded as 2+. Mesentericolumbar collaterals are also shown in the right lower half of the illustration.

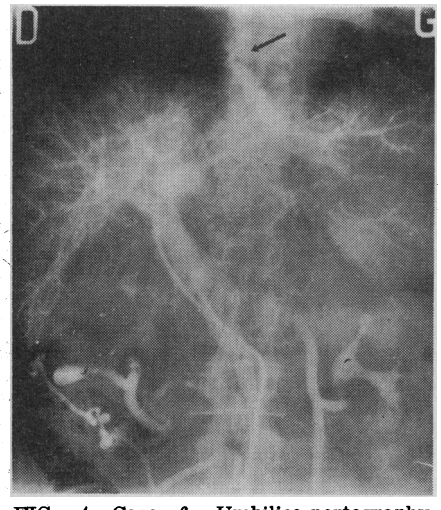

FIG. 4—Case 6. Umbilico-portography (four seconds). The catheter is in the portal vein. Esophageal varices (3+) are seen.

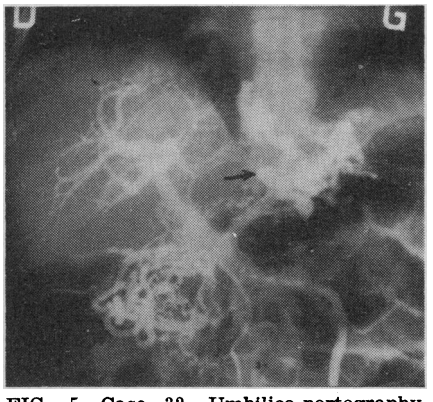

FIG. 5—Case 32. Umbilico-portography (three seconds). Huge gastroesophageal varices from a coronary vein graded as 4+ (upper arrow). Important mesentericolumbar collaterals are also opacified, but not the splenic vein.

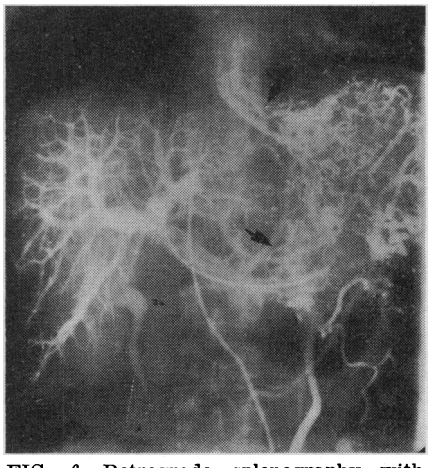

FIG. 6—Retrograde splenography with secondary porto-hepatography (three seconds). The catheter is in the splenic vein. The top arrow shows dye in veins around the gastroesophageal junction arising mostly from the splenic region. Faint opacification of the coronary vein is shown (lower arrow).

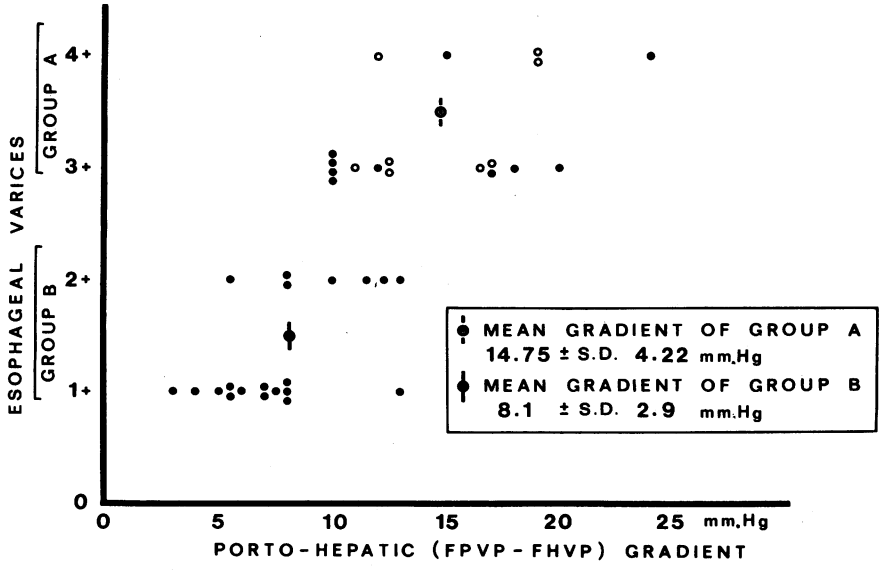

FIG. 7—Correlation between coronary vein involvement and portohepatic gradient in the 38 cirrhotics studied. The open circles represent patients who have bled from ruptured esophageal varices.

Included in this group are the eight patients who bled from their esophageal varices. Evidence for the source of bleeding is indirect. All bleeders had 3+ or 4+ varices on portography. There was no acute or chronic alcohol consumption immediately preceding the bleeding episode. In five (Cases 3, 6, 8, 10 and 29) a liver biopsy, performed between the hemodynamic evaluation and the bleeding episode, did not reveal fatty infiltration. None of the patients were taking salicylates, phenylbutazone, corticosteroid or any related drugs. The upper gastrointestinal radiological studies were all negative for ulcers except in Case 11 where a scarred duodenal cap was described. This last patient was free of ulcer symptoms when bleeding occurred. It is presumed with reasonable certainty that all eight bleeders bled from their varices. The 20 other cirrhotics, none of whom bled from any sources, had coronary vein involvement graded as 1+ or 2+ and formed Group B (Fig. 7 and Table III).

In Group A all 18 cirrhotics had a portohepatic gradient of 10 mm. Hg or more for a mean of 14.75 ± S.D. 4.22 mm. Hg (Table III). Within this group the 10 non-bleeders had a gradient ranging from 10 to 24 mm. Hg for a mean of 14.6 ± S.D. 5.02 mm. Hg, whereas the eight bleeders had a gradient ranging from 11 to 19 mm. Hg for a mean of 14.93 ± S.D. 3.29 mm. Hg. The mean gradient values of the subgroups in Group A showed no statistical difference. In Group B the portohepatic gradient was less than 10 mm. Hg in 15 patients. The range was from 3 to 13 mm. Hg for a mean of 8.1 ± S.D. 2.9 mm. Hg. The difference between the mean gradients of Groups A and B was highly significant ($P < 0.001$).

All patients with 3+ or 4+ CV involvement had a portohepatic gradient equal to or higher than 10 mm. Hg. However, four patients with 2+ CV involvement and one with 1+ CV involvement had a portohepatic gradient equal to or higher than 10 mm. Hg.

There is a highly significant correlation between coronary vein involvement and the portohepatic gradient ($r = 0.7589$, $P < 0.001$).

TABLE II
Summary of radiological and hemodynamic data on the 38 cirrhotic patients

Case no.	*Pressures mm. Hg*			*Portohepatic gradient mm. Hg*	*Position of catheter*	*Gradation of CV involvement*
	FPVP	*WHVP*	*FHVP*	*FPVP-FHVP*		
1	16.0	16.0	6.0	10.0	PV	+++
2	13.5	13.5	8.0	5.5	PV	+
3	26.5	30.0	10.0	16.5	PV	+++
4	28.5	28.0	17.0	11.5	PV	++
5	17.5	18.0	9.0	8.5	PV	+
6	19.0	20.0	6.5	12.5	PV	+++
7	31.5	28.5	13.5	18.0	PV	+++
8	25.0	25.0	6.0	19.0	PV	++++
9	34.0	33.0	10.0	24.0	PV	++++
10	25.5	25.5	13.0	12.5	PV	+++
11	26.0	26.0	9.0	17.0	PV	+++
12	20.0	20.5	10.0	10.0	PV	+++
13	20.5	21.0	15.5	5.0	PV	+
14	24.0	24.0	7.0	17.0	PV	+++
15	18.0	18.0	8.0	10.0	PV	++
16	18.0	16.5	6.0	12.0	PV	++
17	24.0	22.0	12.0	12.0	PV	+++
18	9.0	9.5	5.0	4.0	PV	+
19	13.0	13.0	7.5	5.5	PV	++
20	19.0	19.0	10.0	9.0	PV	+
21	25.0	24.0	10.0	15.0	PV	++++
22	13.0	14.0	7.0	6.0	PV	+
23	28.0	28.0	17.0	11.0	PV	+++
24	17.0	16.0	9.0	8.0	PV	+
25	24.0	20.0	11.0	13.0	PV	++
26	34.0	34.0	14.0	20.0	PV	+++
27	20.0	21.0	12.0	8.0	PV	++
28	17.0	18.0	8.0	9.0	PV	+
29	31.0	31.0	19.0	12.0	PV	++++
30	19.0	19.0	11.0	8.0	PV	++
31	15.0	14.0	12.0	3.0	PV	+
32	38.0	40.0	19.0	19.0	PV	++++
33	12.0	12.0	2.0	10.0	PV	+++
34	16.0	14.0	6.0	10.0	PV	+++
35	24.0	23.5	15.0	9.0	PV	+
36	23.0	23.0	10.0	13.0	PV	+
37	25.0	25.5	17.0	8.0	PV	+
38	11.0	11.0	5.5	5.5	PV	+

Discussion

Umbilicoportal catheterization is one of the most useful approaches in the evaluation of portal hypertension. Combined with hepatic vein catheterization, it permits precise hemodynamic evaluation of this syndrome, excellent radiological data and the measurement of hepatic blood flow.[5, 6]

By simple hepatic vein catheterization good hemodynamic data can be obtained with recordings of WHVP and FHVP (the former is identical or almost so to FPVP in cirrhosis)[10] but radiography of the portal system is not possible. By using only portal catheterization, excellent radiographs are easy to obtain but hepatic blood flow and

TABLE III
Hepatic and umbilicoportal catheterization in 38 cirrhotic patients: hemodynamic and radiological data

	Group A			*Group B*
	Total	*Non-bleeders*	*Bleeders*	
FPVP-FHVP mm. Hg	(n = 18)	(n = 10)	(n = 8)	(n = 20)
Range	10-24	10-24	11-19	3-13
Mean	14.75	14.6	14.93	8.1
S.E.	0.99	1.58	1.16	0.65
S.D.	4.22	5.02	3.29	2.9
Mean grade of coronary vein involvement	3.22+	3.35+	3.37+	1.35+

Group A: 3+ or 4+ esophageal varices
Group B: 1+ or 2+ esophageal varices
FPVH-FHVP: Free portal venous pressure—free hepatic venous pressure gradient

related studies cannot be performed and the hemodynamic data are not as reliable.

In Cases 35, 36 and 37, there is a high FPVP and 1+ varices. Since the FHVP is also high, the elevated pressures are the results of increased intra-abdominal pressure at the time of the recording and/or setting the zero baseline too low. The use of the portohepatic gradient (FPVP-FHVP) as an index of portal hypertension eliminates both these sources of error.[11]

In the present study all the patients who have bled from esophageal varices were found to belong to Group A, with 3+ or 4+ coronary vein involvement and with a portohepatic gradient of 10 mm. Hg or more. In this group, 10 patients had not bled from esophageal varices at the time of the study. These patients may be referred to as "potential bleeders". (In fact, since this paper was prepared, one of these "potential bleeders" has bled from esophageal varices and has had a successful portocaval shunt.)

The importance of other collaterals, such as those opacified by retrograde splenography, must be considered in the total evaluation of patients with portal hypertension, but these could not be taken into account in the present study since retrograde splenography was not performed in all patients. Our group is currently supplementing its evaluation of such cases with retrograde splenography and esophagoscopy.

The criteria suggested by Conn,[4] when applied to the selection of patients to be submitted to prophylactic shunt, resulted in a definite improvement in the survival rate of a group now studied for four years.

A clear definition of the high-risk patients is imperative in the evaluation of cirrhotics with esophageal varices if prophylactic portocaval shunts are to be usefully performed.

In conclusion, there is a significant correlation between the size of coronary vein varices and the portohepatic gradient. There is also a significant correlation between the presence of large varices with a portohepatic gradient of 10 mm. Hg or more and a high risk of variceal bleeding. The radiological and hemodynamic data obtained by combined hepatic and umbilicoportal catheterization in cirrhosis of the liver can be of valuable help in the selection of potential bleeders.

Résumé

Hémorragie par rupture de varices œsophagiennes chez les cirrhotiques: identification des sujets en danger d'hémorragie à l'aide de critères hémodynamiques et radiologiques obtenus par cathétérisme hépatique et ombilicoportal

Trente-huit cirrhotiques compensés ont subi un cathétérisme hépatique et ombilicoportal. Une porto-hépatographie fut obtenue dans tous les cas et l'atteinte de la veine coronaire fut appréciée séparément (1+ à 4+). La pression portale libre (PPL), la pression sus-hépatique bloquée (PSHB) et la pression sus-hépatique libre (PSHL) furent enrégistrées. Le gradient porto-hépatique (PPL-PSHL) fut utilisé comme critère d'hypertension portale.

Dix-huit des malades étudiés étaient porteurs de varices 3+ ou 4+ (groupe A) et tous présentèrent un gradient porto-hépatique d'au moins 10 mm. Hg. Des 20 autres cirrhotiques (varices 1+ et 2+ ou groupe B), 15 présentèrent un gradient porto-hépatique de moins de 10 mm Hg. Une différence hautement significative entre les gradients du groupe A et du groupe B fut retrouvée.

Huit des malades étudiés ont présenté une hémorragie par rupture de varices œsophagiennes et tous se retrouvent dans le groupe A. Cependant, il n'existe pas de différence significative entre le gradient de ces huit malades et le gradient des 10 autres malades du groupe A.

Il existe une corrélation significative entre la présence de grosses varices œsophagiennes avec un gradient porto-hépatique égal ou supérieur à 10 mm Hg et un risque élevé d'hémorrhagie par varices œsophagiennes. Les données radiologiques et hémodynamiques obtenues par le cathétérisme hépatique et ombilicoportal dans la cirrhose du foie peuvent être d'une grande utilité dans l'identification des cirrhotiques présentant un danger d'hémorragie par rupture de varices œsophagiennes.

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