

CASOS CLÍNICOS

Varón
57 años
HCV crónico
en fase cirrótica



Manometría portal

PSO: 11

PSL: 4

GPS: 7

(N: \leq 5 mmHg)



Manometría portal

PSO: 16

PSL: 3

GPS: 13

(N: \leq 5 mmHg)

Varón

63 años

**HCV crónico en fase
cirrótica**

Manometría portal

PSO: 20

PSL: 3

GPS: 17

(N: \leq 5 mmHg)



Manometría portal

PSO: 21

PSL: 3

GPS: 18

(N: \leq 5 mmHg)



Varón

56 años

Trombosis portal

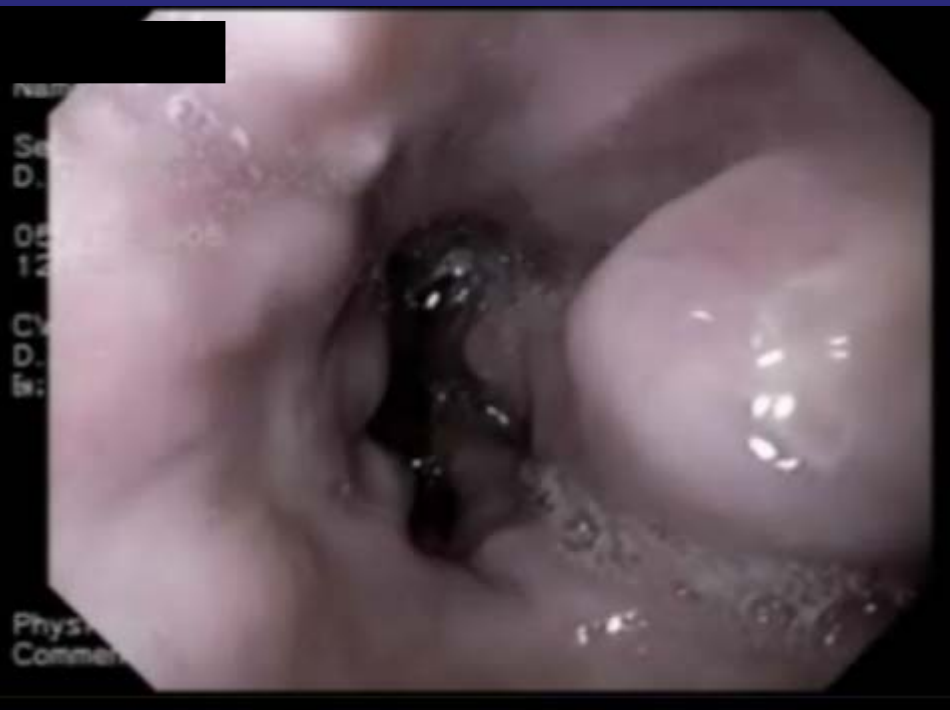
Manometría portal

PSO: 9

PSL: 5

GPS: 4

(N: \leq 5 mmHg)



Pre tratamiento farmacológico

Post-tratamiento farmacológico

Manometría portal

PSO: 20

PSL: 5

GPS: 15

Manometría portal

PSO: 19

PSL: 5

GPS: 14

No respondedor

Pre tratamiento farmacológico

Post-tratamiento farmacológico

Manometría portal



PSO: 20

PSL: 5

GPS: 15

Manometría portal



PSO: 14

PSL: 6

GPS: 8



>20%

VF < 12 mmHg

Pre tratamiento farmacológico

Post-tratamiento farmacológico

Manometría portal

PSO: 23

PSL: 5

GPS: 18

Manometría portal

PSO: 19

PSL: 5

GPS: 14

 > 20%

VF > 12 mmHg

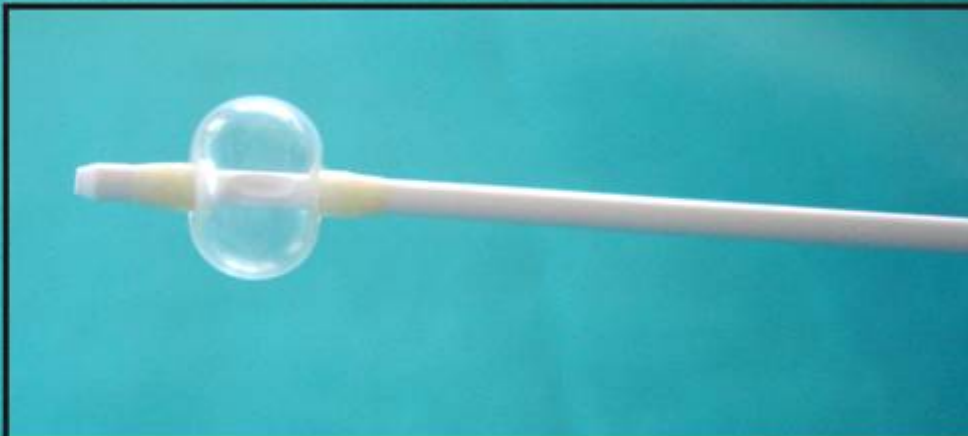
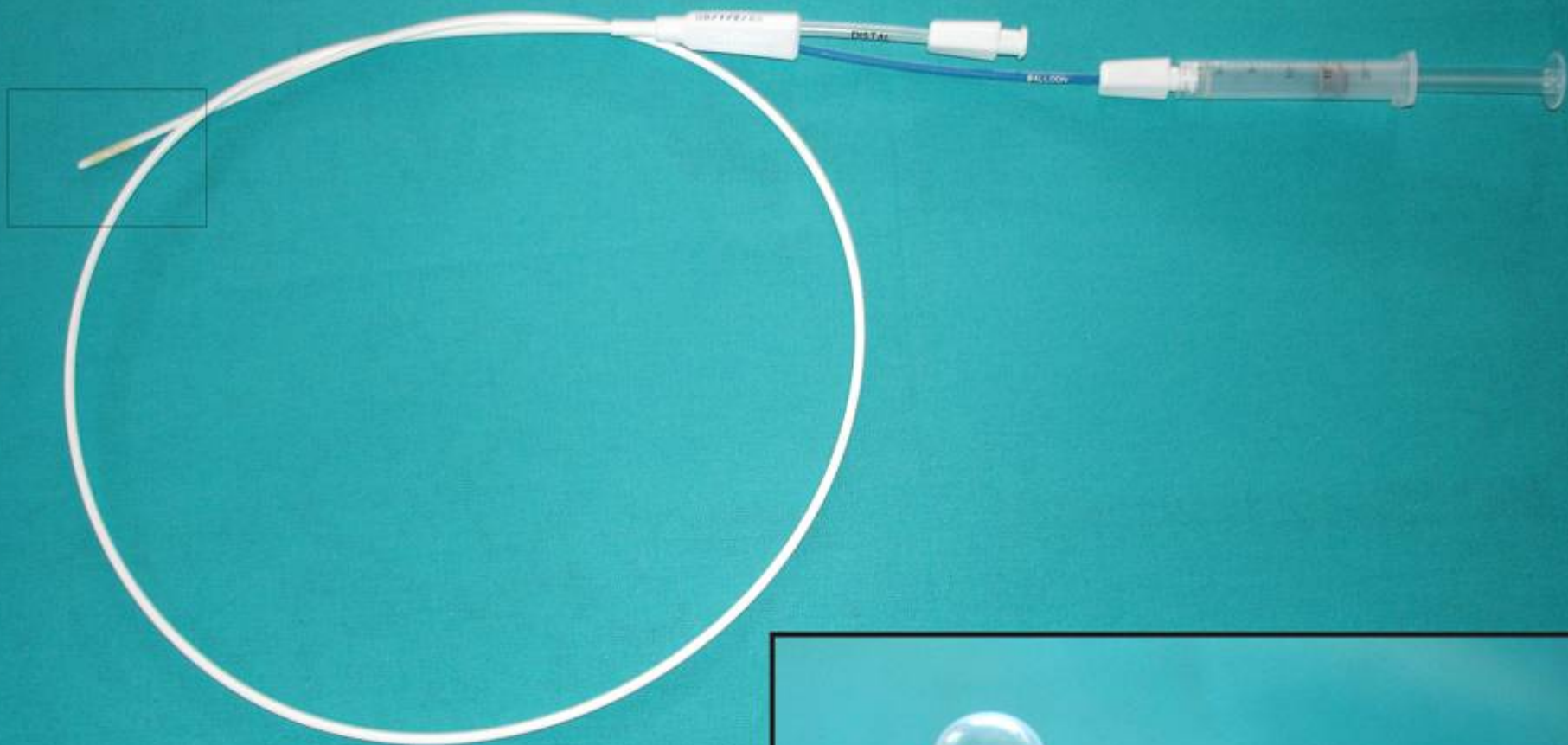


**Symposium Honoring
Roberto J. Groszmann, M.D.
New Haven. November 7, 2007**

**HVPG in practice.
How, when and why?**

**Julio Vorobioff, M.D.
University of Rosario Medical School**

HOW TO DO IT



Groszmann RJ et al; Gastroenterology 1979

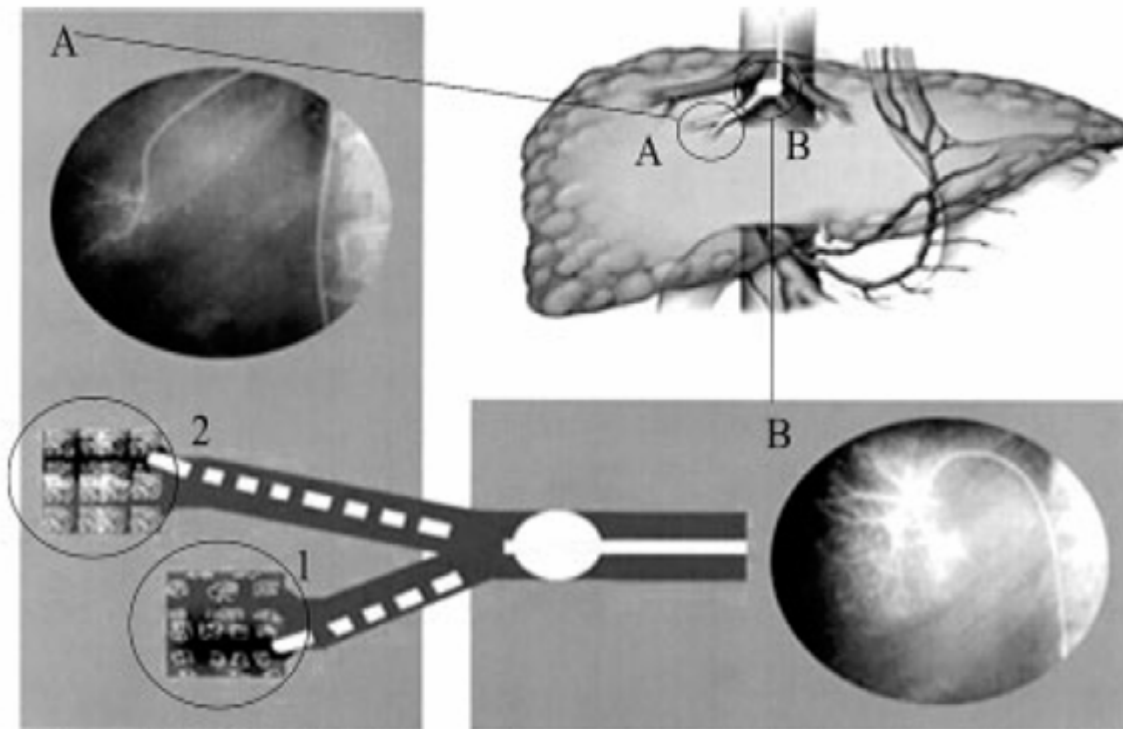


Fig. 1. (A) The pressure transducer on the straight catheter is wedged into a small hepatic vein. Because there is a regional variability of fibrosis, the WHVP of the more fibrotic area (**inset 1**) is higher than that of the relatively normal parenchyma (**inset 2**). (B) The balloon catheter eliminates this inconsistency by averaging WHVP over a wider segment of the liver.

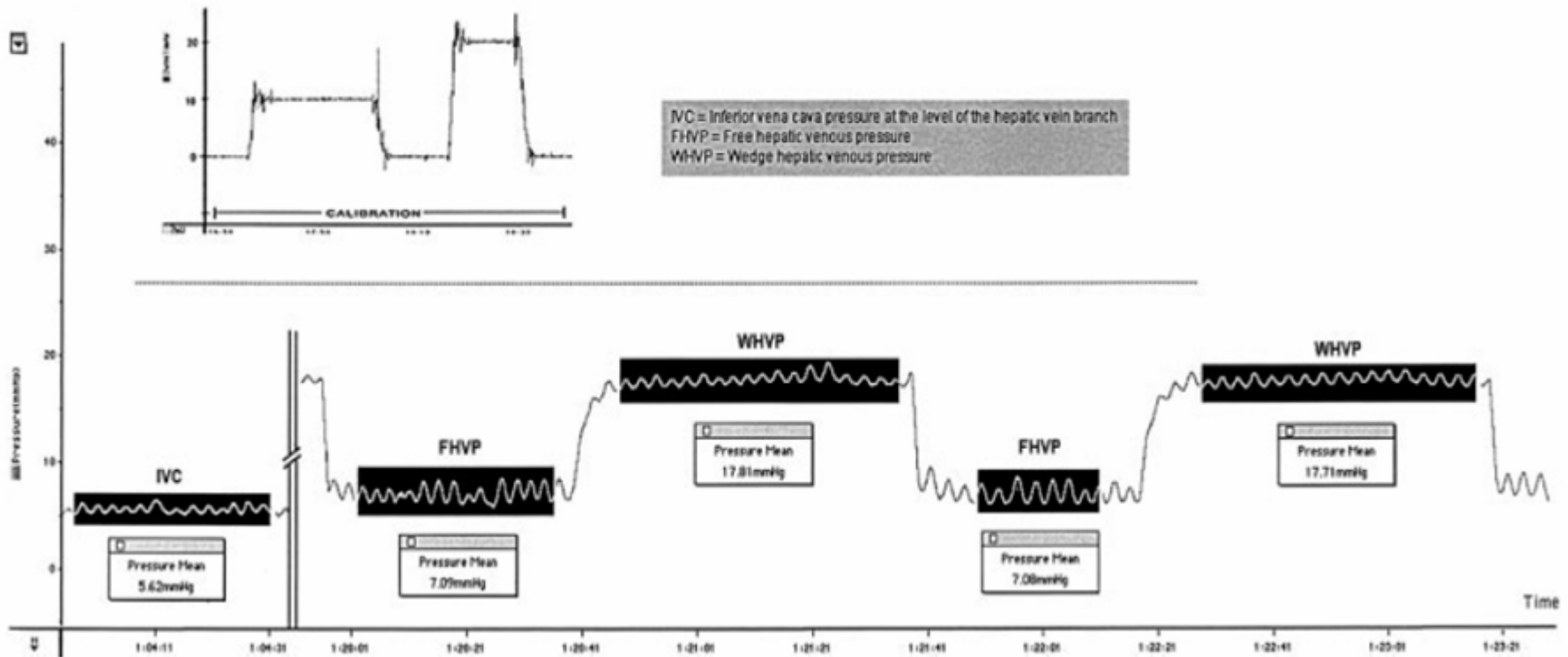
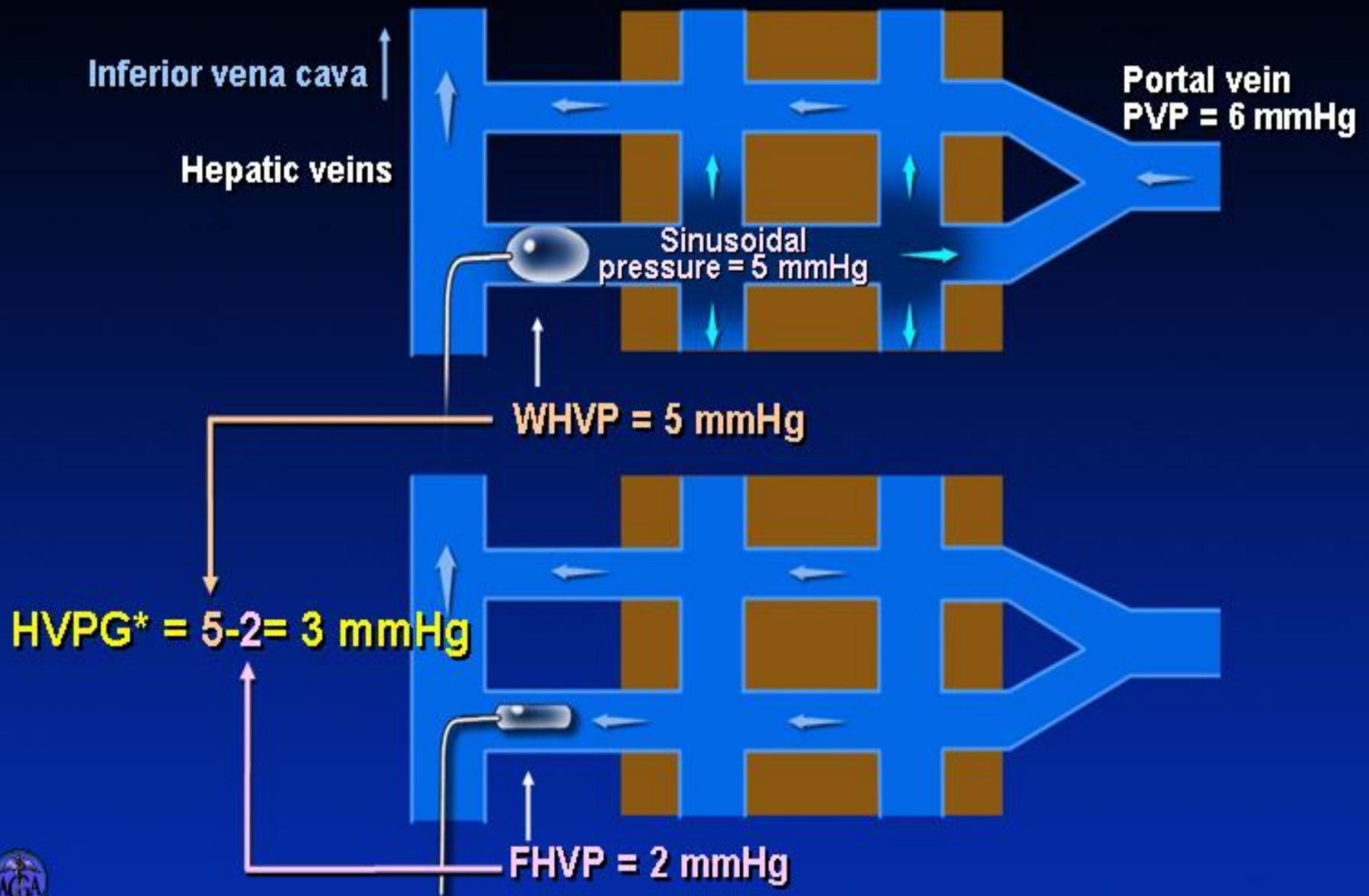


Fig. 2. The pressure transducer needs to be calibrated carefully against known external pressure. **(Top)**, a 13.6-cm and a 27.2-cm column of water are used to calibrate the transducer to 10 and 20 mm Hg, respectively. Pressure readings are obtained by averaging values of stable tracings as shown in the highlighted area. We use the arithmetic function built into the tracing recorder to calculate the mean pressures for the inferior vena cava (IVC), FHVP, and WHVP. A stable tracing of 45 to 60 seconds is necessary for WHVP measurement whereas a tracing of 15 to 20 seconds is adequate for IVC and FHVP measurement.

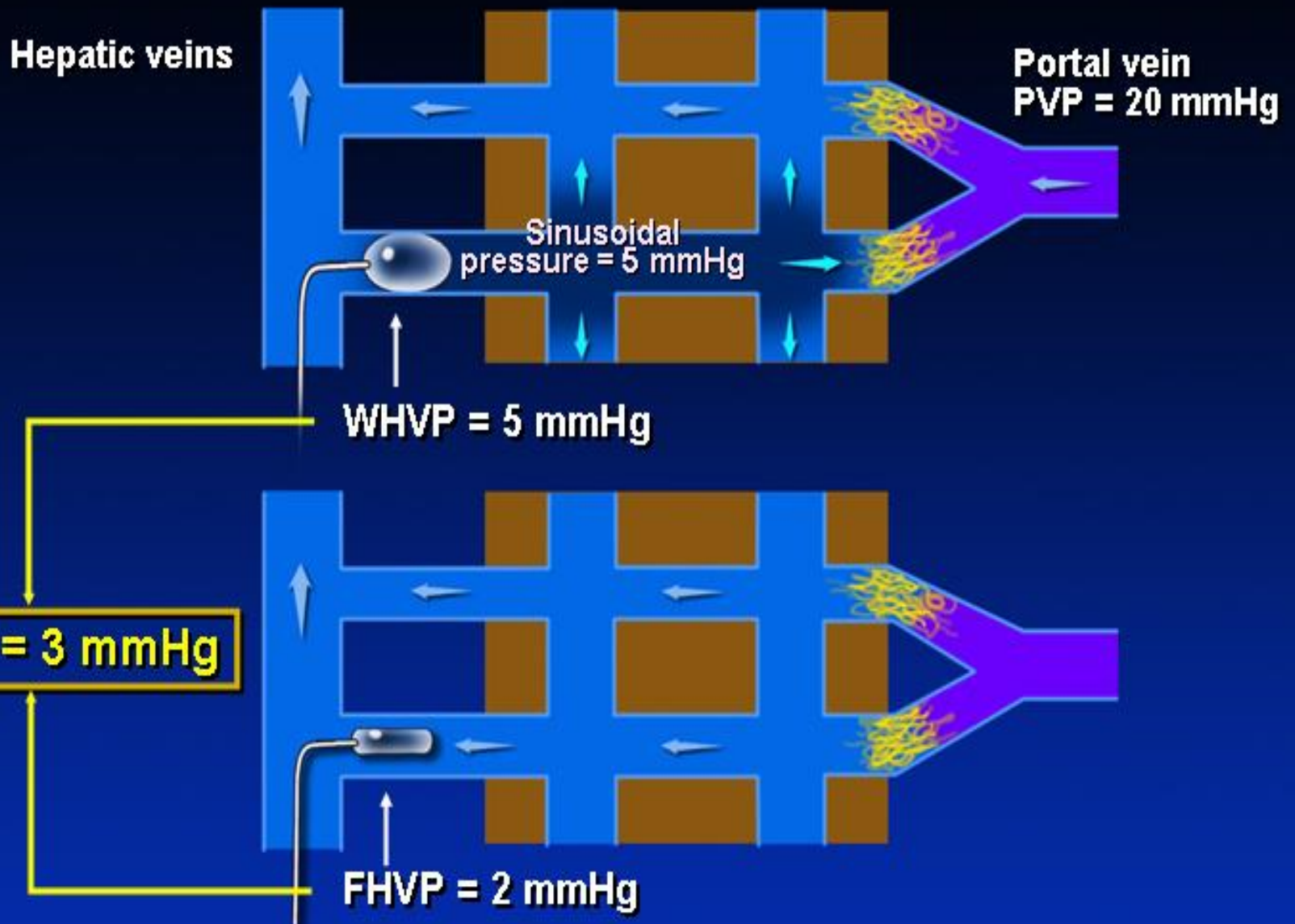
WHEN TO DO IT

DIAGNOSIS OF PORTAL HYPERTENSION

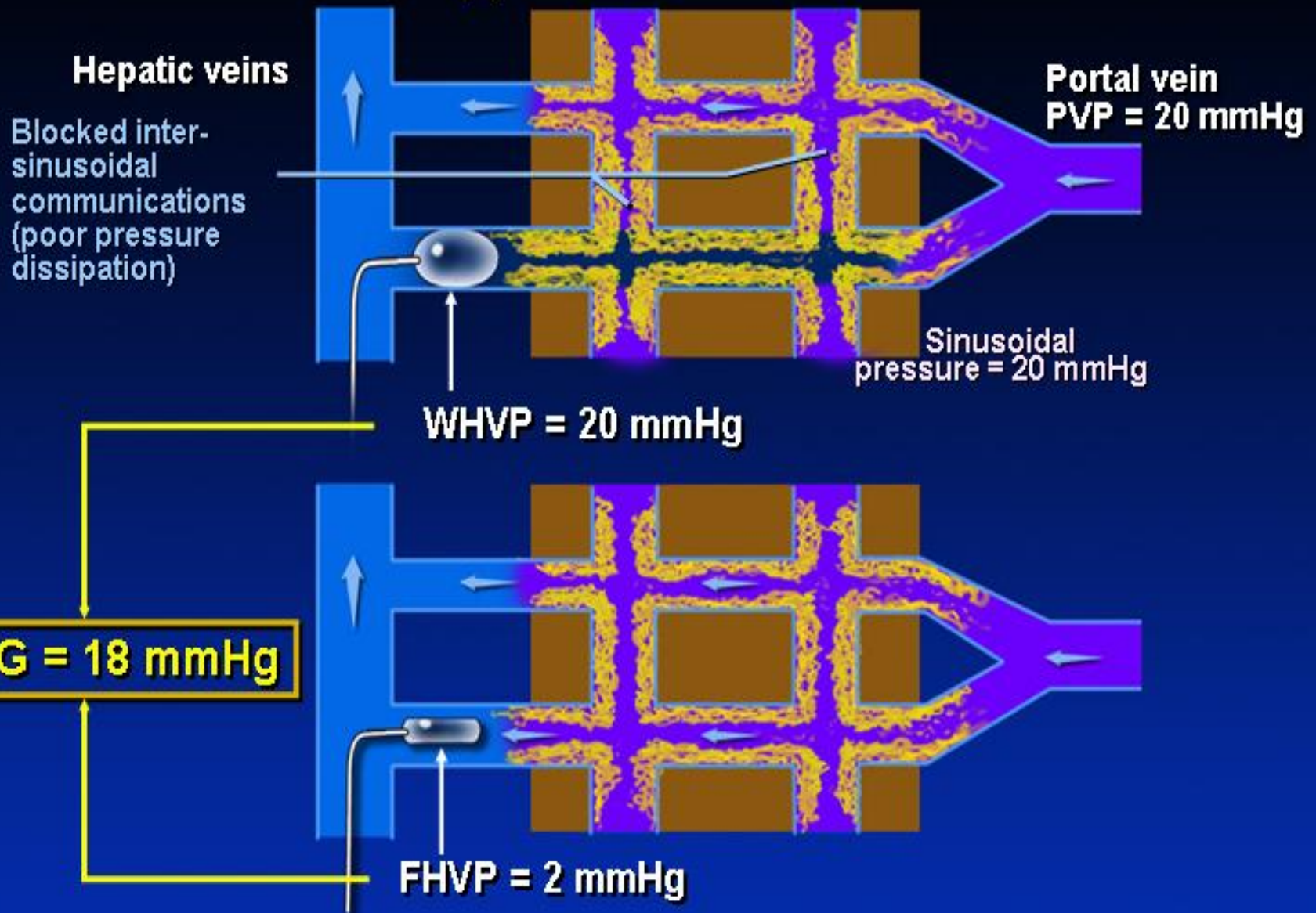
Normal HVPG is 3-5 mmHg



HVPG is Normal in Presinusoidal Portal Hypertension

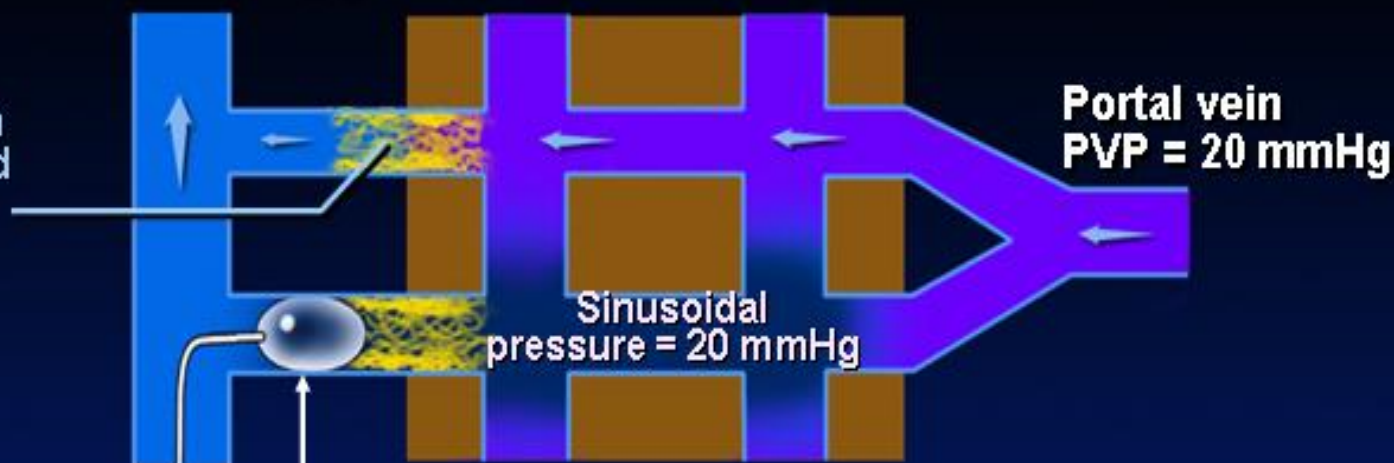


HVPG is Increased in Sinusoidal Portal Hypertension



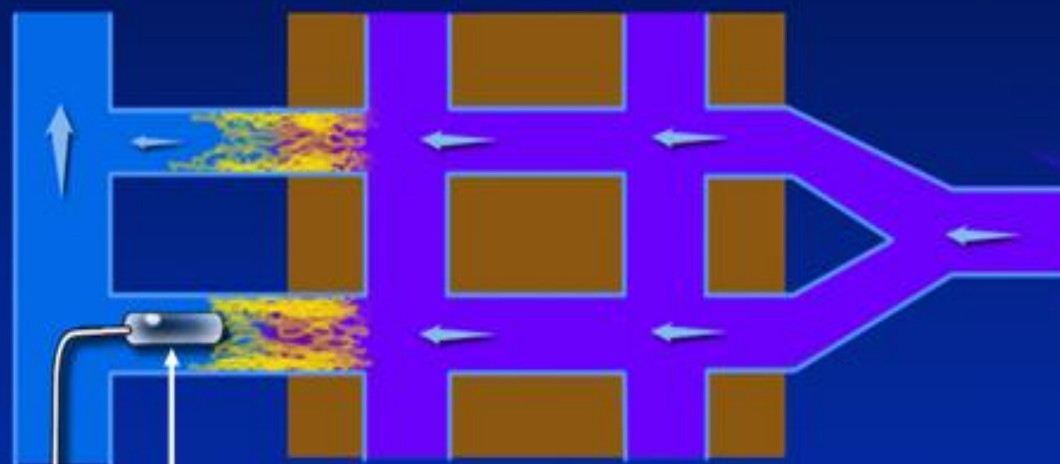
HVPG is Increased in Post-Sinusoidal Portal Hypertension

Outflow obstruction even in non-wedged hepatic vein (poor pressure dissipation)



WHVP = 20 mmHg

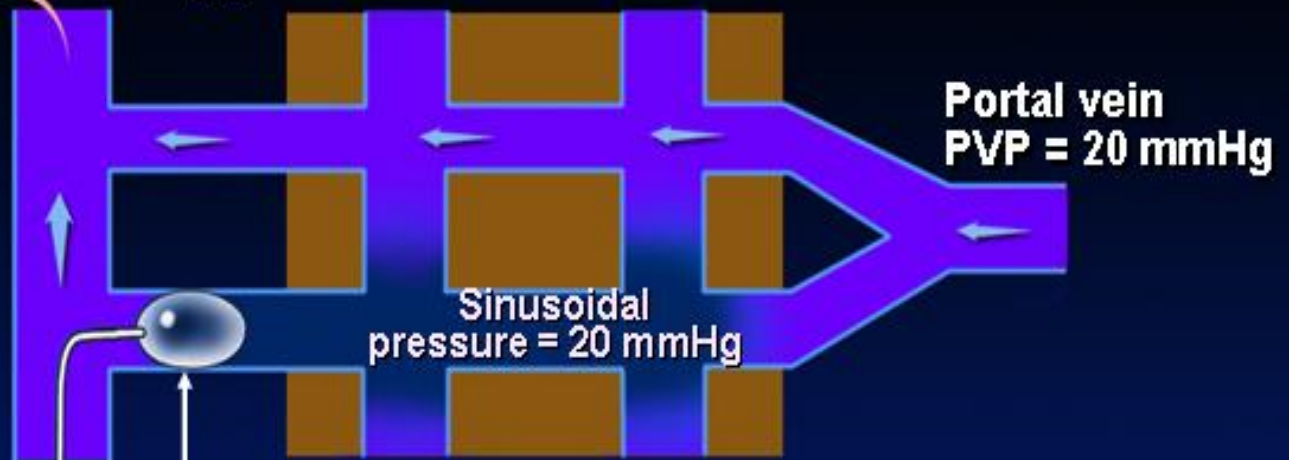
HVPG = 18 mmHg



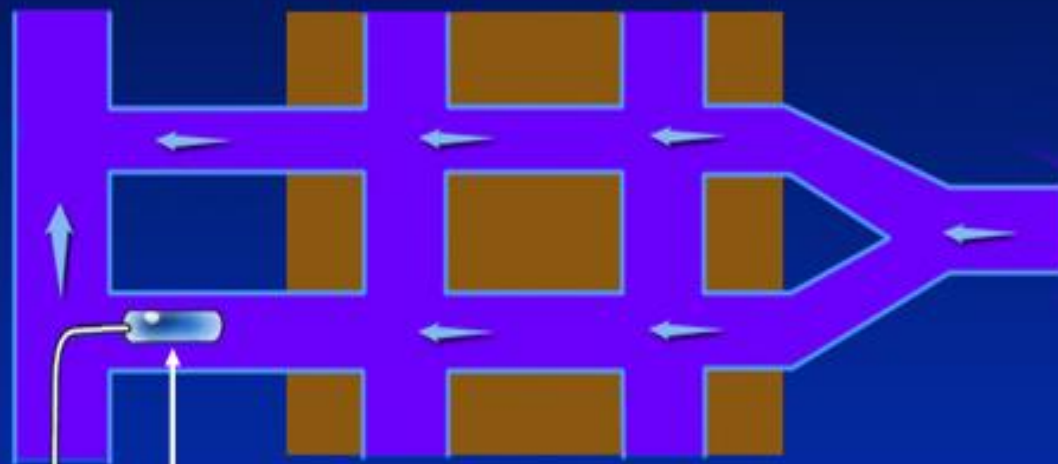
FHVP = 2 mmHg



HVPG is Normal in Post-Hepatic Portal Hypertension



WHVP = 20 mmHg



FHVP = 18 mmHg

HVPG = 2 mmHg



Hepatic Venous Pressure Gradient (HVPG) in the Differential Diagnosis of Portal Hypertension

Type of Portal Hypertension	Wedged (WHVP)	Free (FHVP)	Gradient (HVPG)
Pre-hepatic	normal	normal	normal
Pre-sinusoidal	normal	normal	normal
Sinusoidal	↑	normal	↑
Post-sinusoidal	↑	normal	↑
Post-hepatic			
• Heart failure	↑	↑	normal
• Budd-Chiari	unable to catheterize hepatic vein		



**PREDICTION OF
COMPLICATIONS
OF PORTAL
HYPERTENSION**

DEVELOPMENT OF
VARICES AND
CLINICAL
DECOMPENSATION

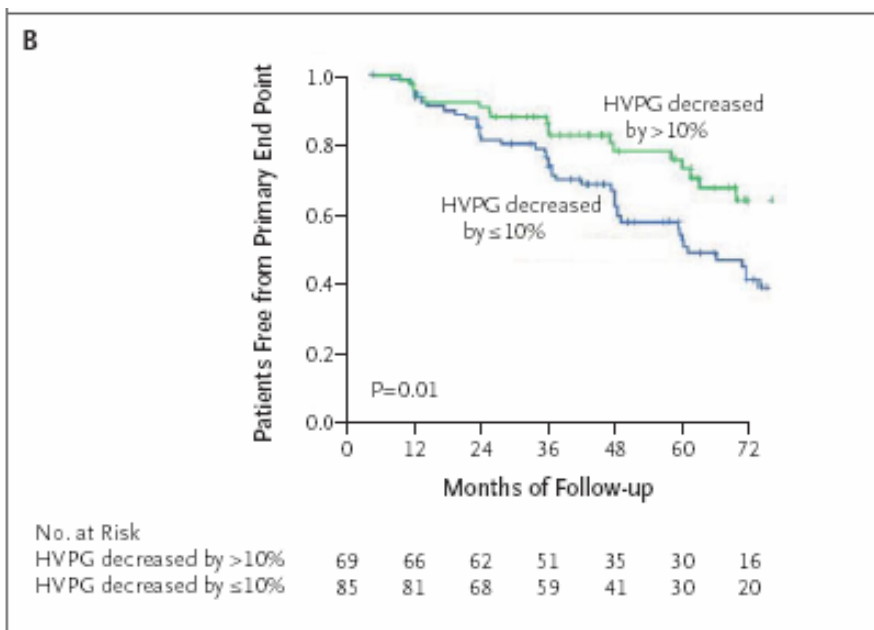
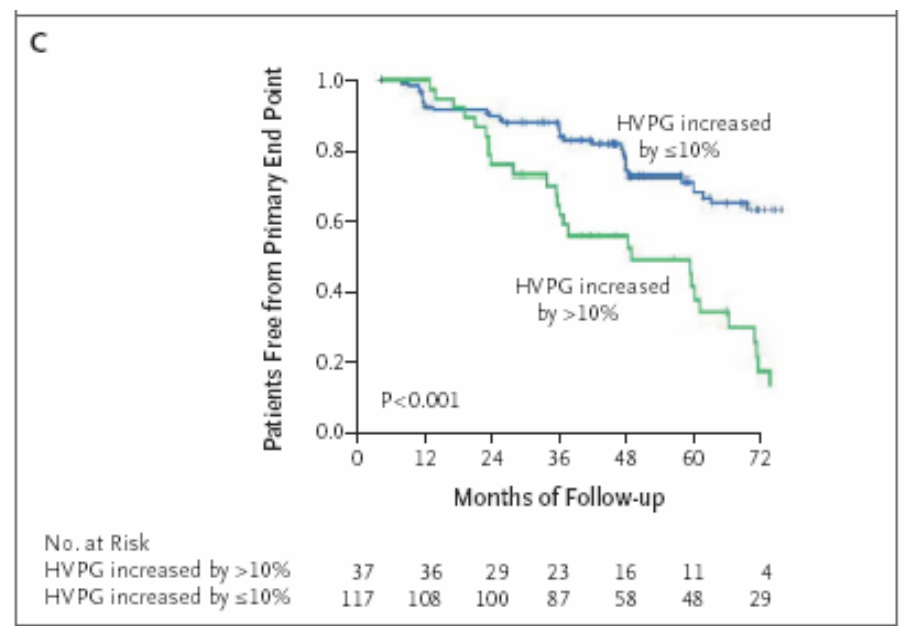
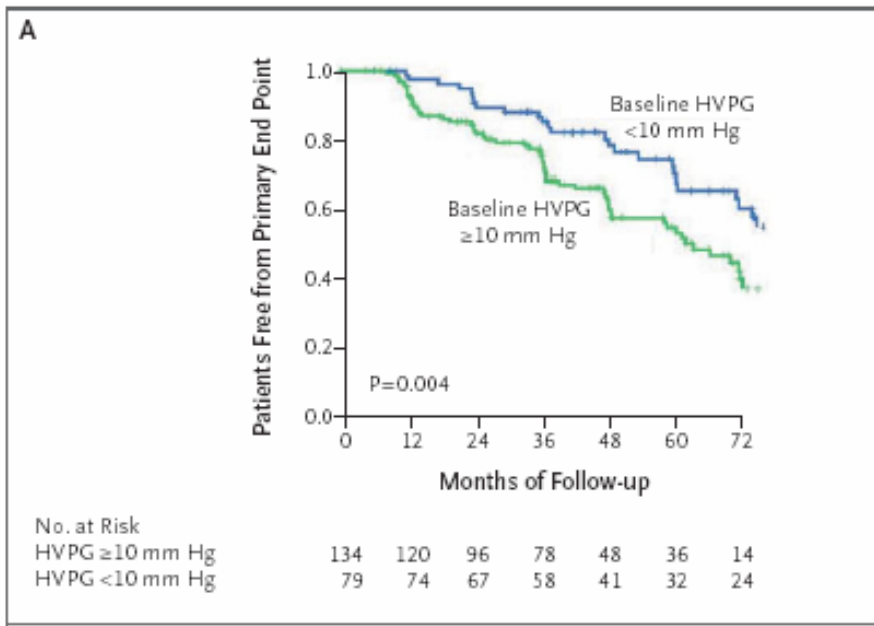
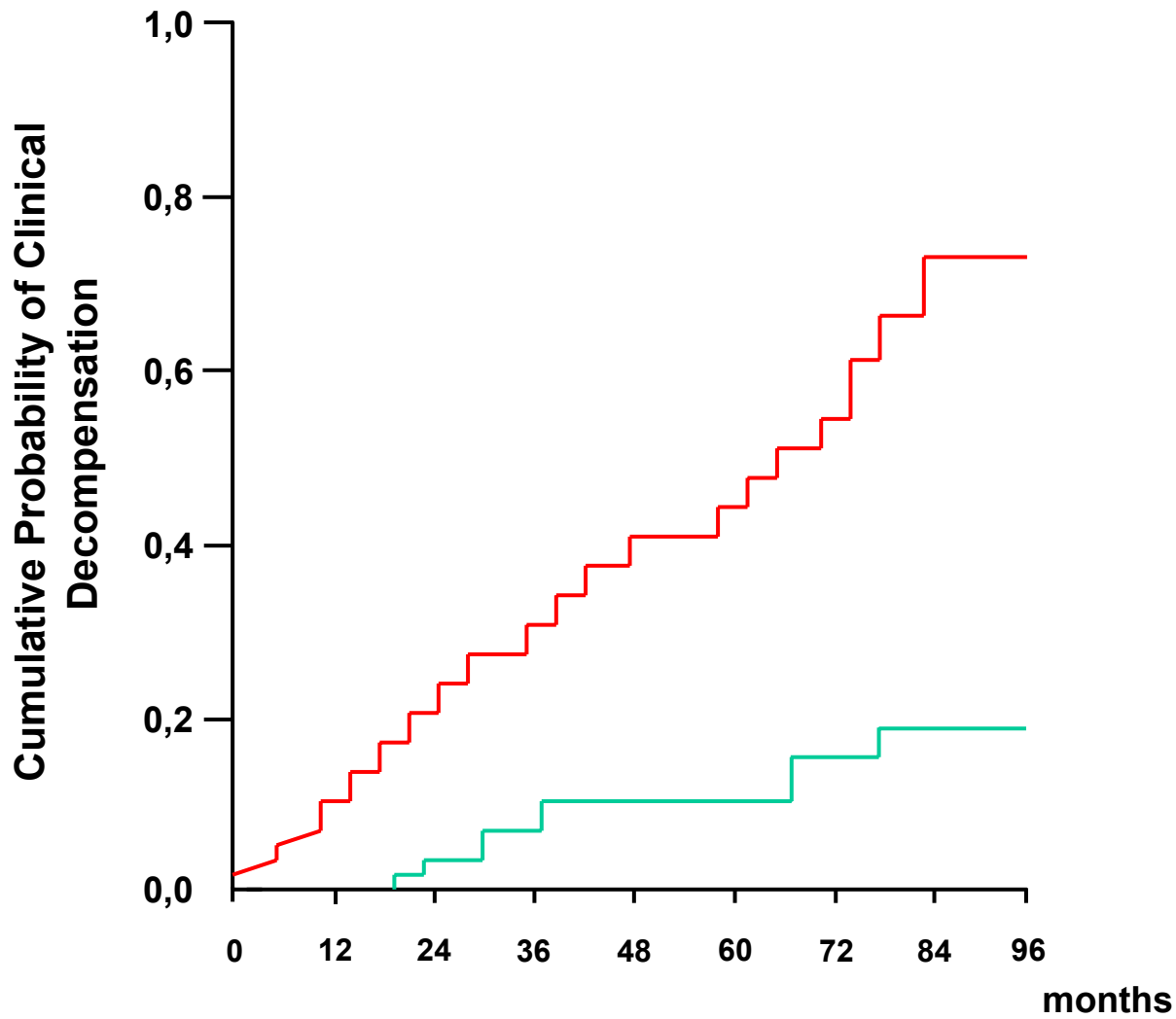


Figure 3. Probability of Remaining Free of the Primary End Point of Varices or Variceal Bleeding, According to the HVPG at Baseline (Panel A) and the Presence or Absence of Either a Decrease in HVPG by More Than 10 Percent (Panel B) or an Increase in HVPG by More Than 10 Percent (Panel C) at One Year.



HVPg < 10 mmHg

At risk	79	72	66	55	44	32	14
Events	0	0	2	4	6	6	8

HVPg ≥ 10 mmHg

At risk	134	112	86	73	49	34	3
Events	0	15	29	33	44	47	54

TO PREDICT
VARICEAL
BLEEDING

HVPG and variceal bleeding

- A HVPG of 12 mmHg is a minimal threshold below which variceal rupture is unlikely

Viallet A et al.; Gastroenterology 1975

García-Tsao G et al.; Hepatology 1985

Rigau J et al.; Gastroenterology 1989

- The HVPG has been shown to be an independent predictor of variceal bleeding

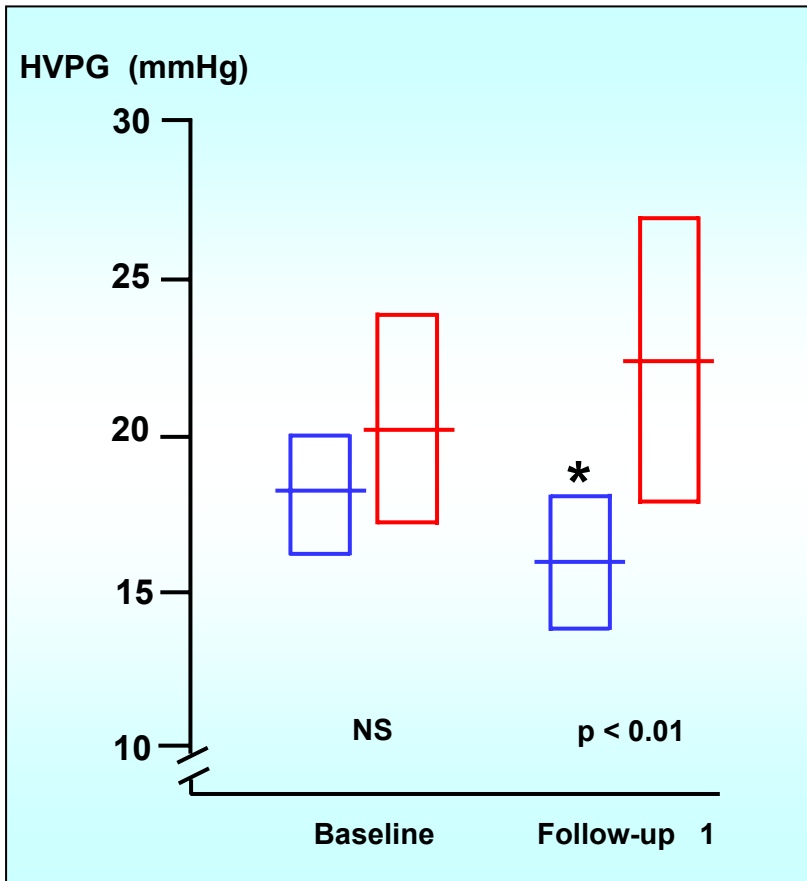
Viola C et al.; J Hepatol 1987

Vlavianos P et al.; Gut 1990

Gluud C et al.; Hepatology 1988

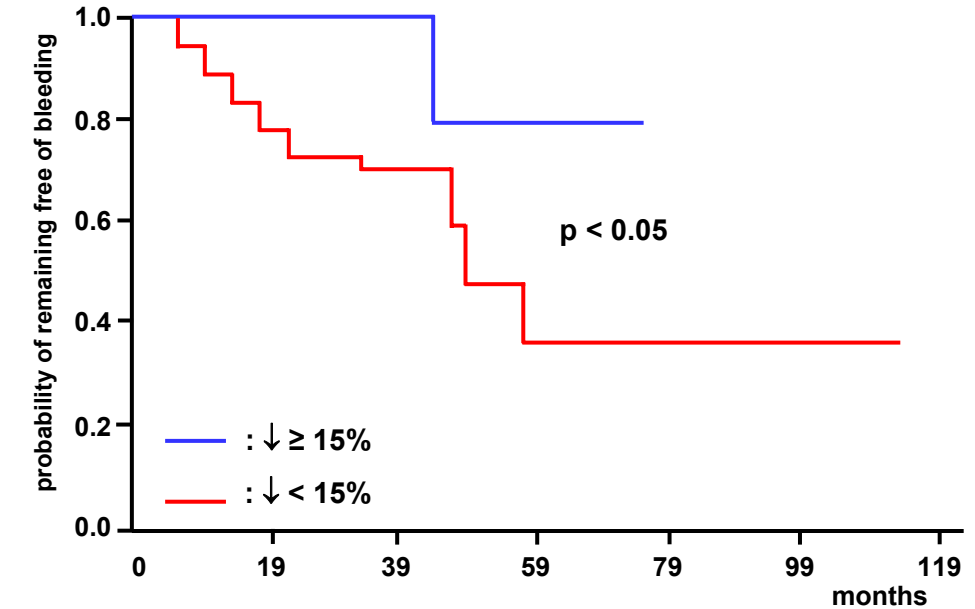
Merkel C et al.; Gastroenterology 1992

Risk of first variceal bleeding



HVPG in non-bleeders (□; n=20) and bleeders (□; n= 10). Compared with baseline value and that in bleeders a significant reduction in HVPG (95 CI) was observed in non-bleeders at follow-up 1 (median, 10 months).

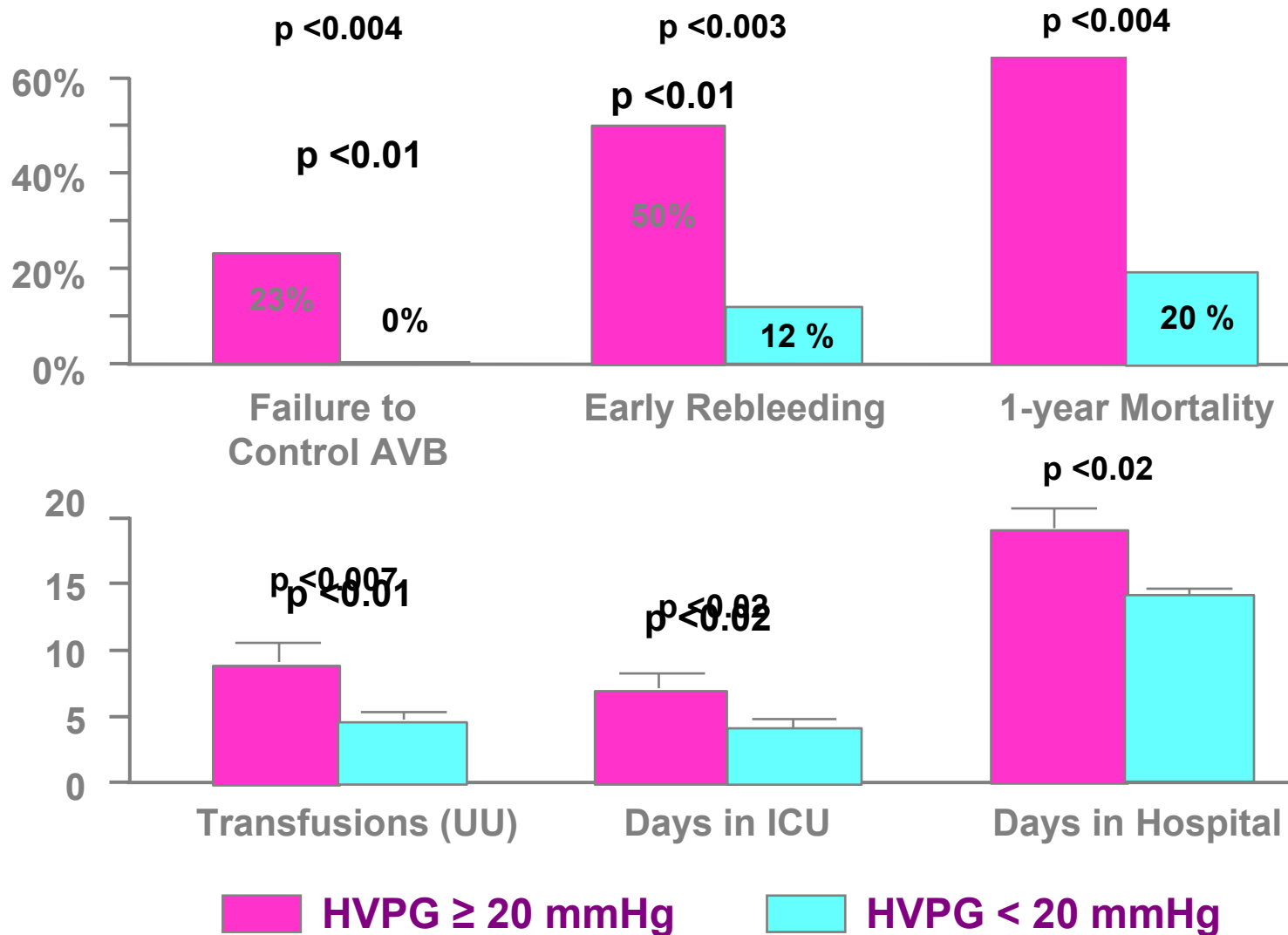
* p > 0.05 vs. baseline



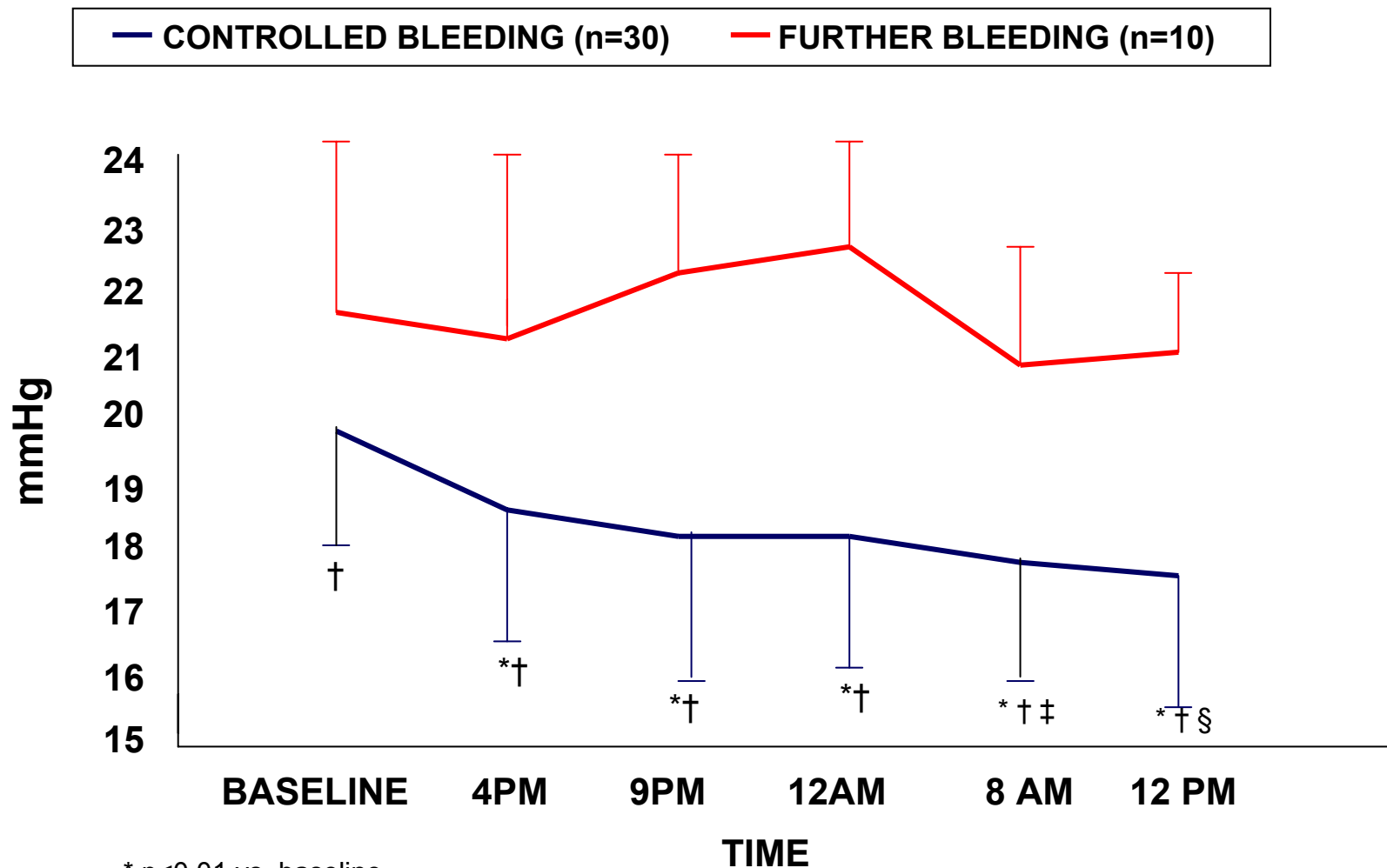
↓ ≥ 15%	11	11	11	10	10		
↓ < 15%	19	14	12	6	5	5	5

Probability of remaining free of bleeding according to changes in HVPG. ↓ ≥ 15%, a decrease of 15% or more; ↓ < 15%, a decrease of less than 15%.

Prognosis in variceal bleeding



Prognosis in variceal bleeding



* $p < 0.01$ vs. baseline

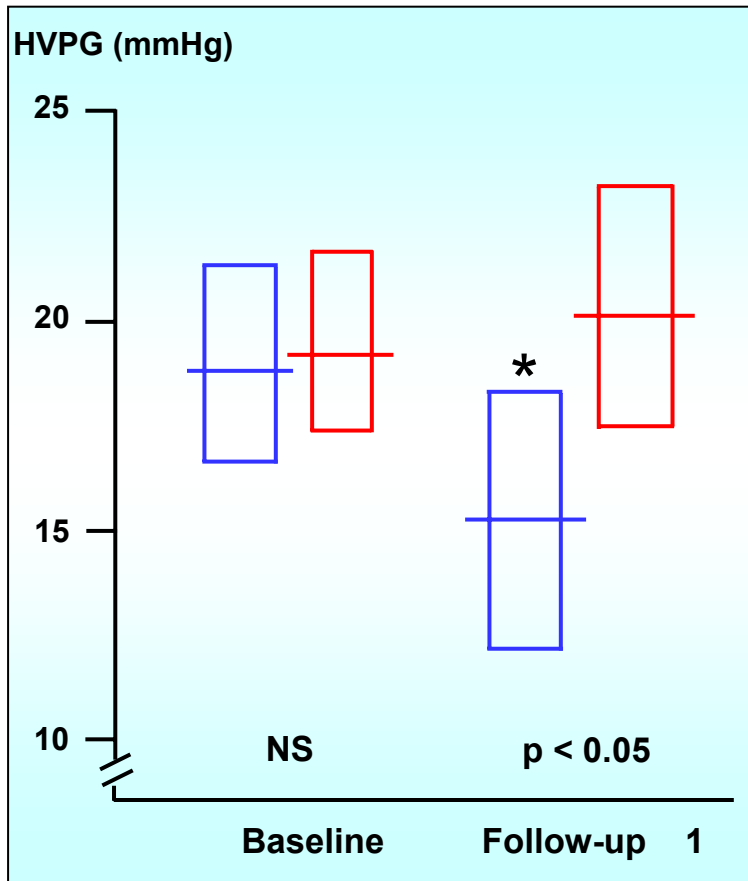
† $p < 0.05$ vs. group with further bleeding

‡ $p < 0.05$ vs. from value at 12 AM

§ $p < 0.05$ vs. from values at 12AM and 4PM

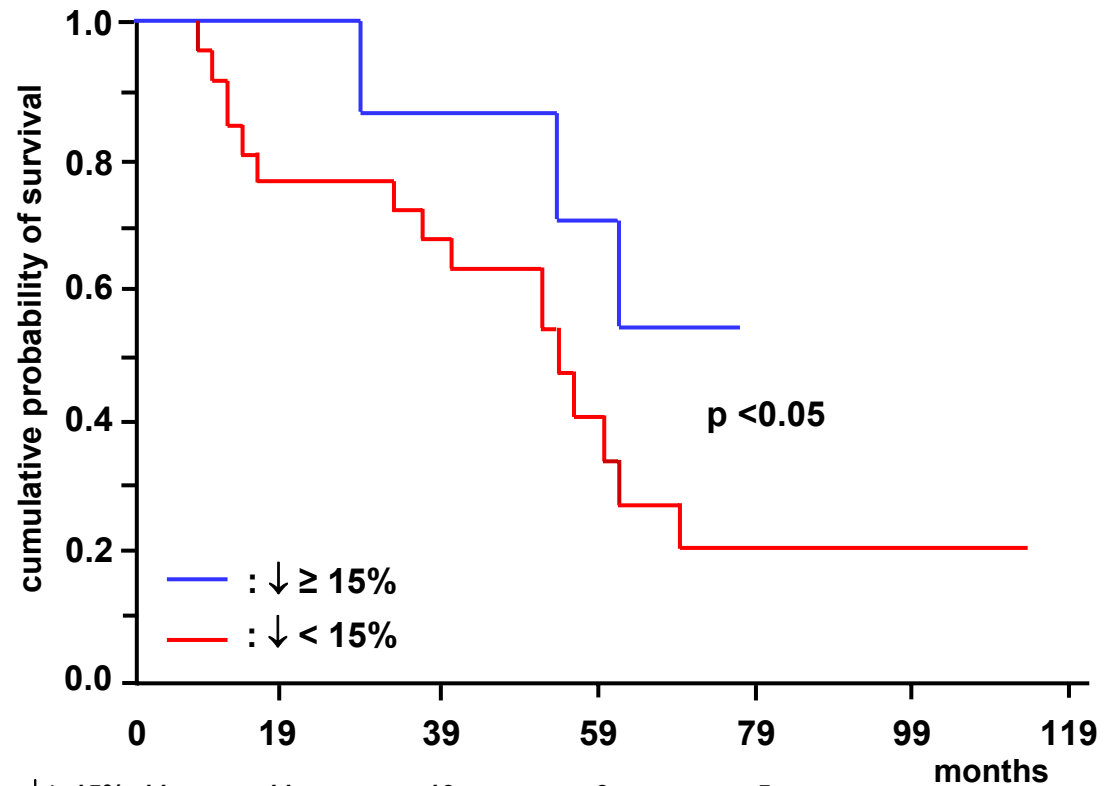
TO PREDICT
SURVIVAL

Survival in previous non-bleeders



HVPG in survivors (□; n=13) and non-survivors (□; n= 17). Compared with baseline value and that in non-survivors a significant reduction in HVPG (95 CI) was observed in survivors at follow-up 1 (median, 10 months).

* p > 0.01 vs. baseline



	0	19	39	59	79	99	119
$\downarrow \geq 15\%$	11	11	10	9	5		
$\downarrow \leq 15\%$	19	14	12	6	5	5	5

Cumulative probability of survival according to changes in HVPG. $\downarrow \geq 15\%$, a decrease of 15% or more; $\downarrow < 15\%$, a decrease of less than 15%.

Survival in active bleeding

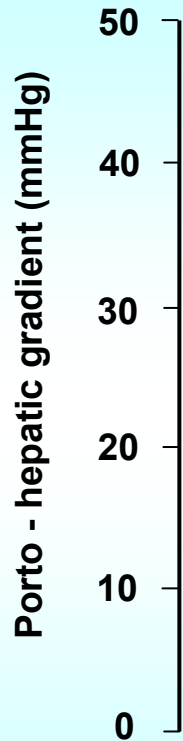


Fig 1. Individual values of portohepatic gradient in 16 bleeders who died during the first 2 weeks (Δ) and in 56 bleeders who survived for at least 2 weeks (\bullet).

TABLE 2. COMPARISON OF MEAN PORTAL PRESSURE VALUES (MEAN \pm S.D.) BETWEEN PATIENTS WHO SURVIVED AT LEAST 1 WEEK, 2 WEEKS OR 1 MONTH, AND PATIENTS WHO DIED WITHIN THE SAME PERIODS OF TIME

		Dead	Survivors	p
1 week	n	12	60	
	PVP	37.2 \pm 7.3	29.1 \pm 8.8	< 0.005
	PHPG	24.6 \pm 8.7	19.8 \pm 8.0	< 0.10
2 weeks	n	16	56	
	PVP	36.5 \pm 6.9	28.6 \pm 8.8	< 0.001
	PHPG	25.6 \pm 8.4	19.0 \pm 7.6	< 0.01
1 month	n	21	51	
	PVP	34.5 \pm 7.4	28.5 \pm 9.1	< 0.01
	PHPG	23.9 \pm 8.0	19.1 \pm 7.9	< 0.025

The abbreviations used are: PVP, portal vein pressure; PHPG, portohepatic pressure gradient.

Survival in previous bleeders

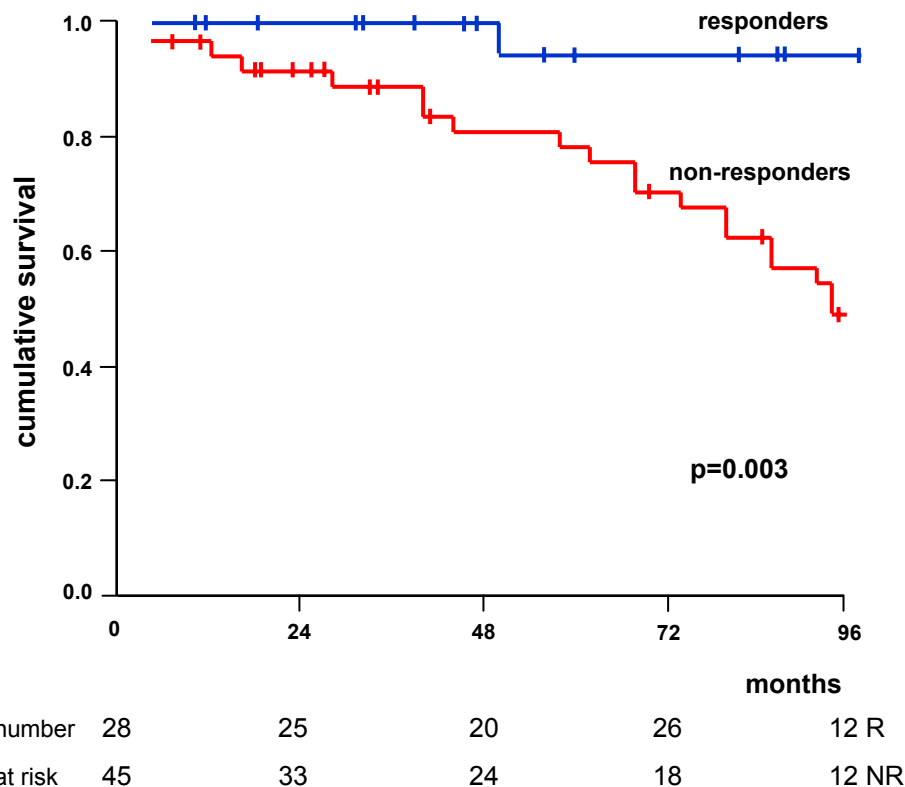


Fig. 5. Eight-year cumulative probability of survival was higher in responders than in nonresponders. Survival difference at 8 years was 43% (95% CI: 21%-63%) (R, responders; NR, nonresponders).

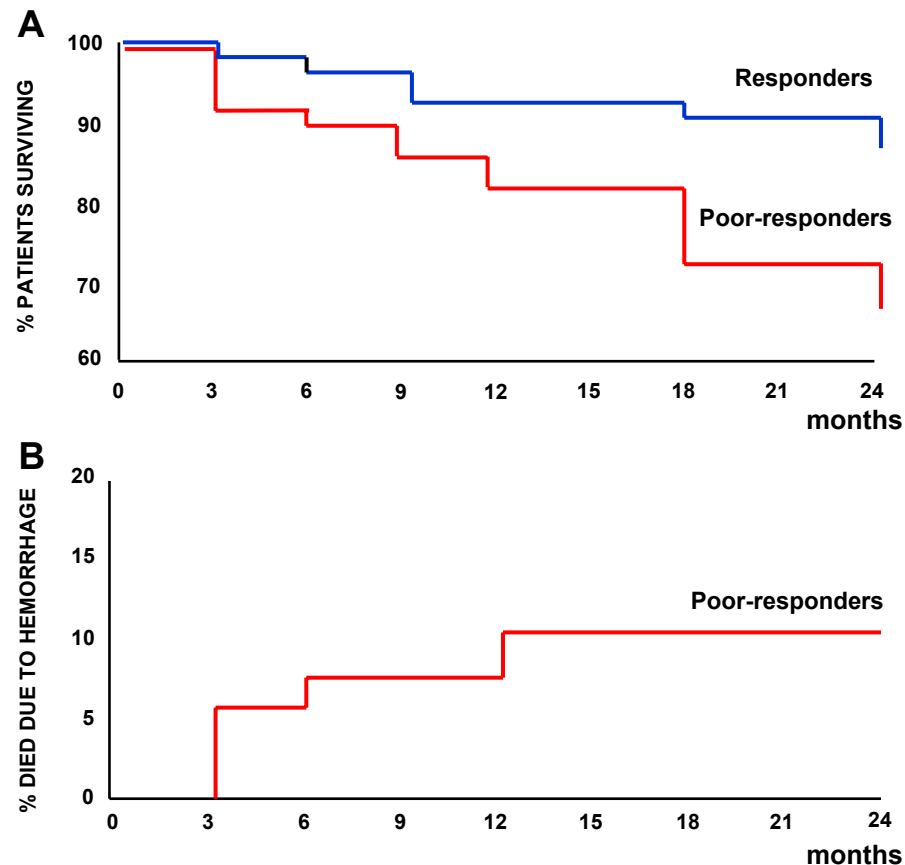
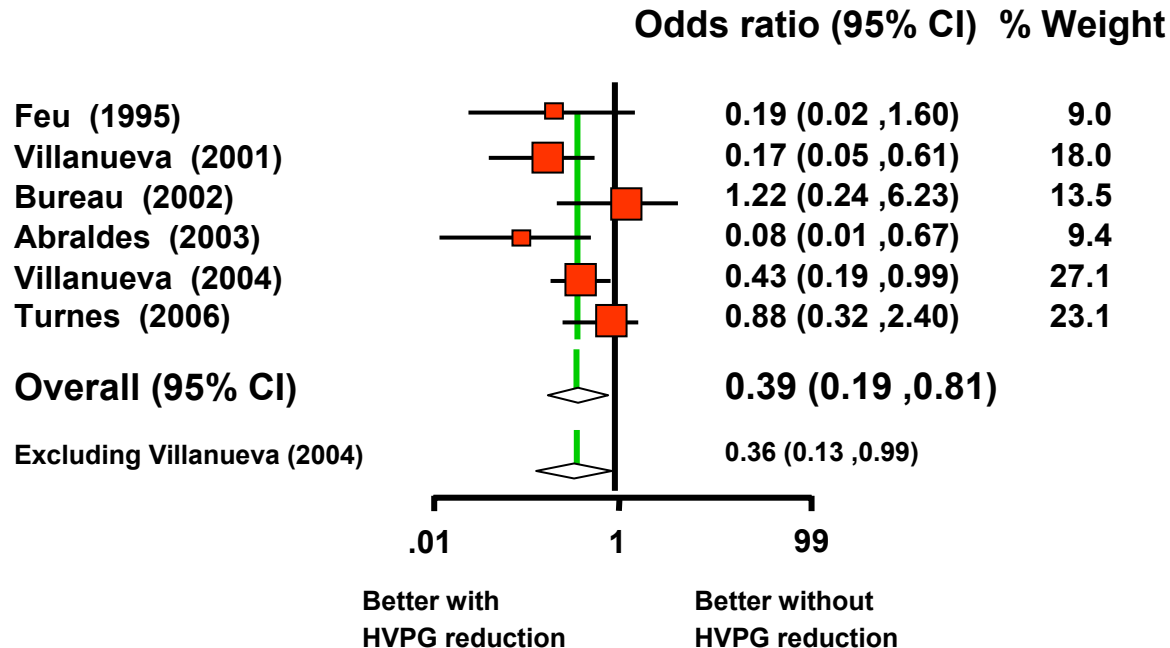


Fig. 4. Actuarial probability of (A) survival and of (B) death due to rebleeding, in both groups of hemodynamic response. (A) The probability of survival was higher among hemodynamic responders than among poor-responders ($P = 0.029$). (B) The probability of death due to rebleeding was lower in responders than in poor-responders ($P = 0.006$).

HVPG and survival

HVPG was predictive of death in 67% of 117 prognostic studies in cirrhosis in which this parameter was analyzed.

D'Amico G et al.; J Hepatol 2006



Odds ratio for the risk of death in patients with and, respectively, without HVPG reduction by $\geq 20\%$ or to ≤ 12 mmHg

D'Amico G et al.; Gastroenterology 2006

PHARMACOLOGIC THERAPY

EFFICACY ASSESSMENT

PRIMARY
AND
SECONDARY
PROPHYLAXIS

Prevention of first variceal hemorrhage

Decrease of HVPG

≤ 12 mm Hg (n:21)

> 12 mm Hg (n:63)

Patients free of bleeding (cumulative %)

100

71 ± 14

$p < 0.05$

Patients surviving (cumulative %)

≤ 12 mm Hg (n:21)

> 12 mm Hg (n:63)

86 ± 13

32 ± 24

$p < 0.05$

Change in variceal size

≤ 12 mm Hg (n:21)

> 12 mm Hg (n:63)

$- 0.62 \pm 0.97$

$- 0.08 \pm 0.75$

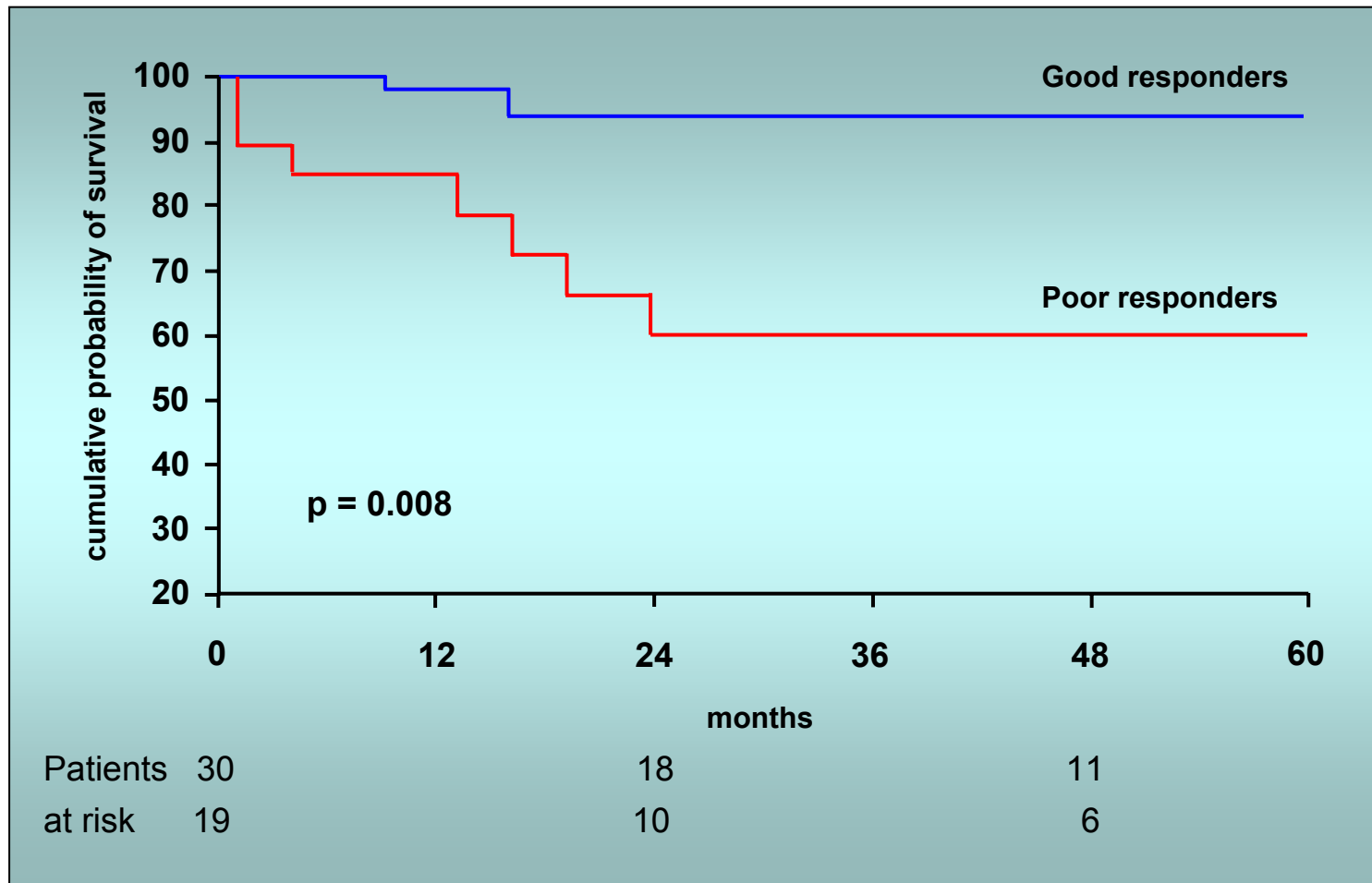
$p < 0.01$

Hemodynamic Response to Propranolol and Incidence of Variceal Rebleeding

Response of HVPG (% change from baseline)	Rebleeding on Follow-Up	
None or increase	9 / 17	(53%)
< 10% decrease	6 / 11	(54%)
10–20% decrease	8 / 16	(50%)
≥ 20% decrease		
- final HVPG > 12 mmHg	2 / 17	(12%)
- final HVPG ≤ 12 mmHg	0 / 8	(0%)

chi-square = 13.914, p<0.01

Risk of first variceal hemorrhage



Cumulative probability of being free of first variceal bleeding in good responders (-) and poor responders (-) according to hemodynamic Criteria.

Risk of late rebleeding

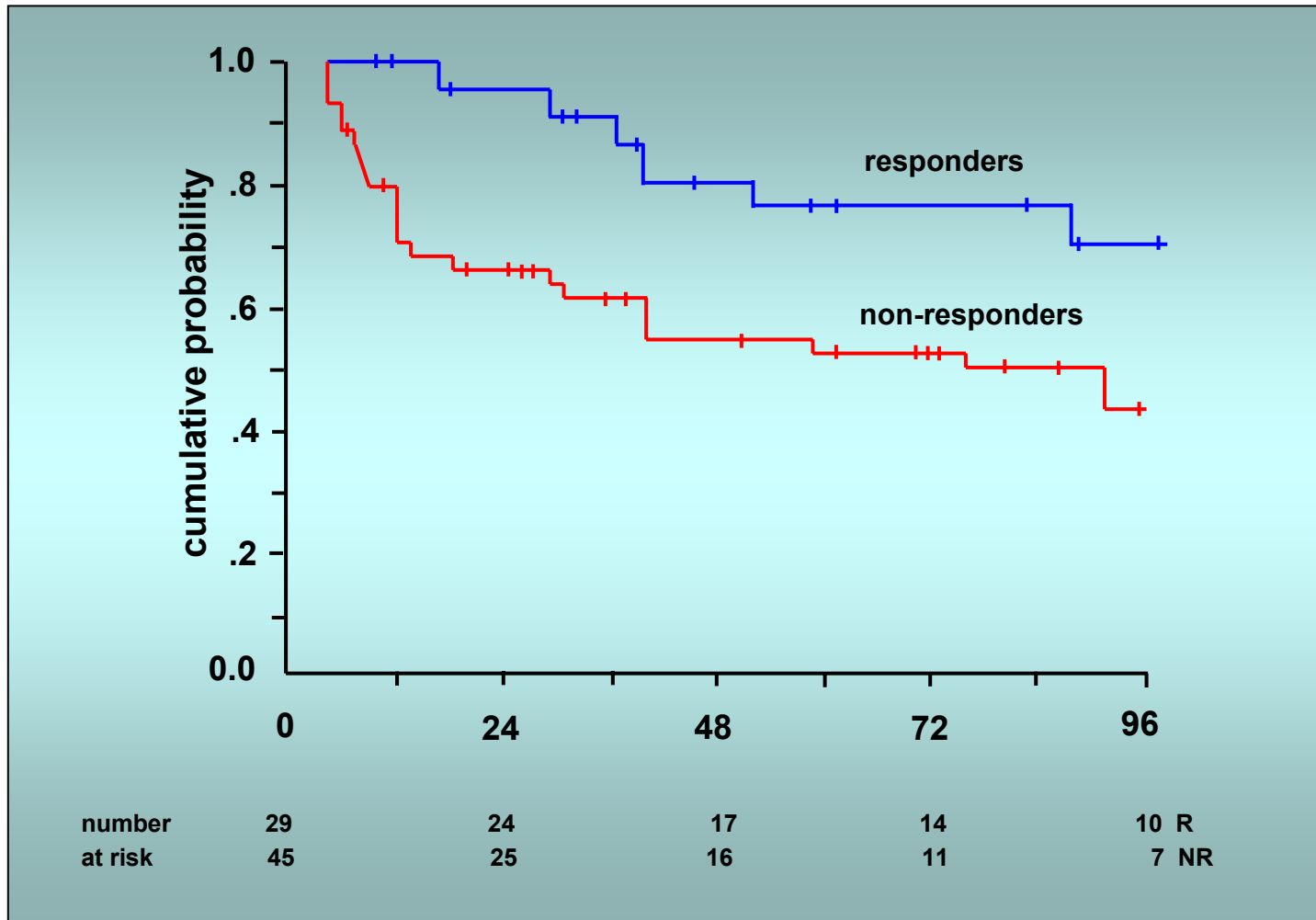
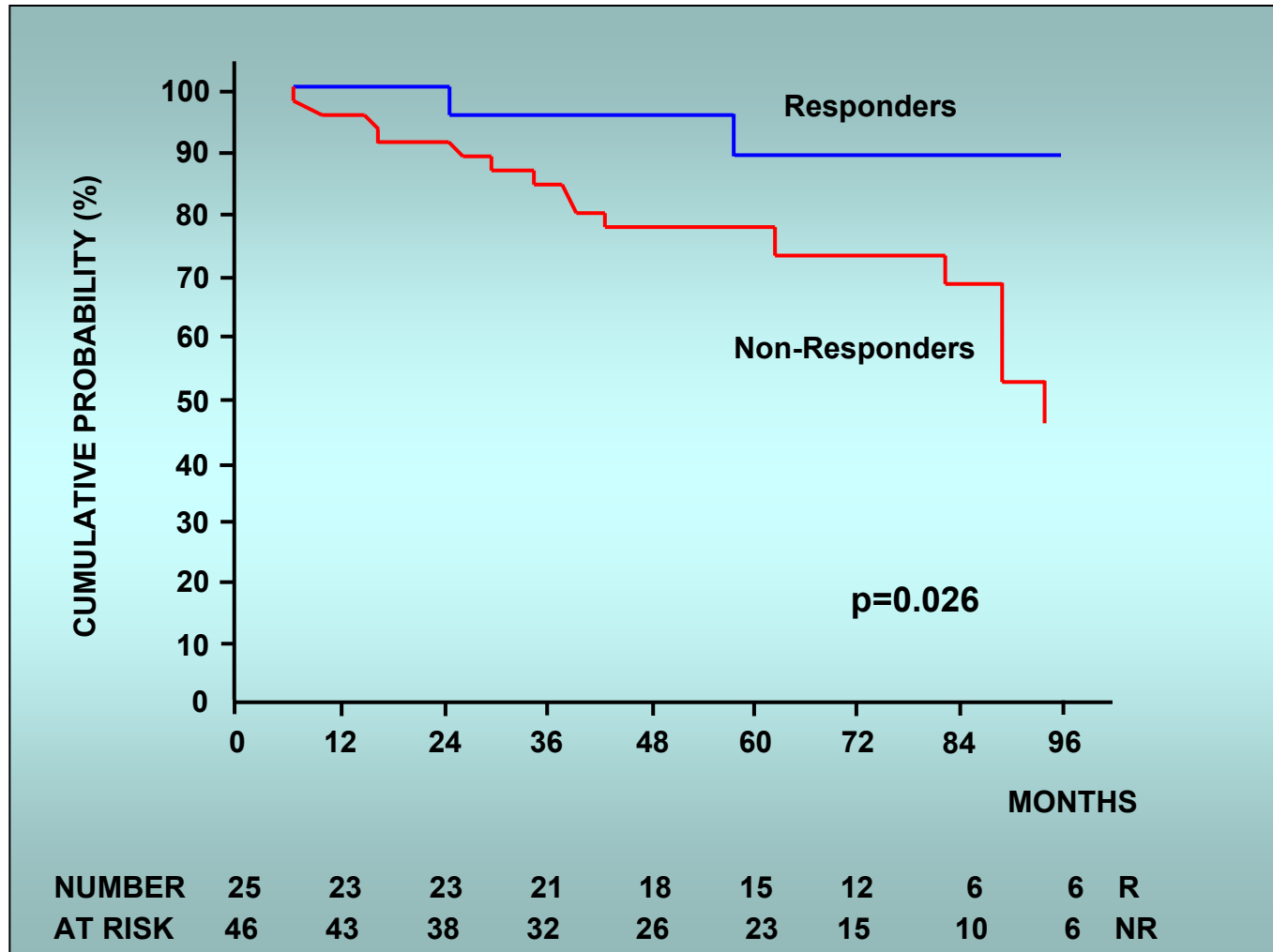


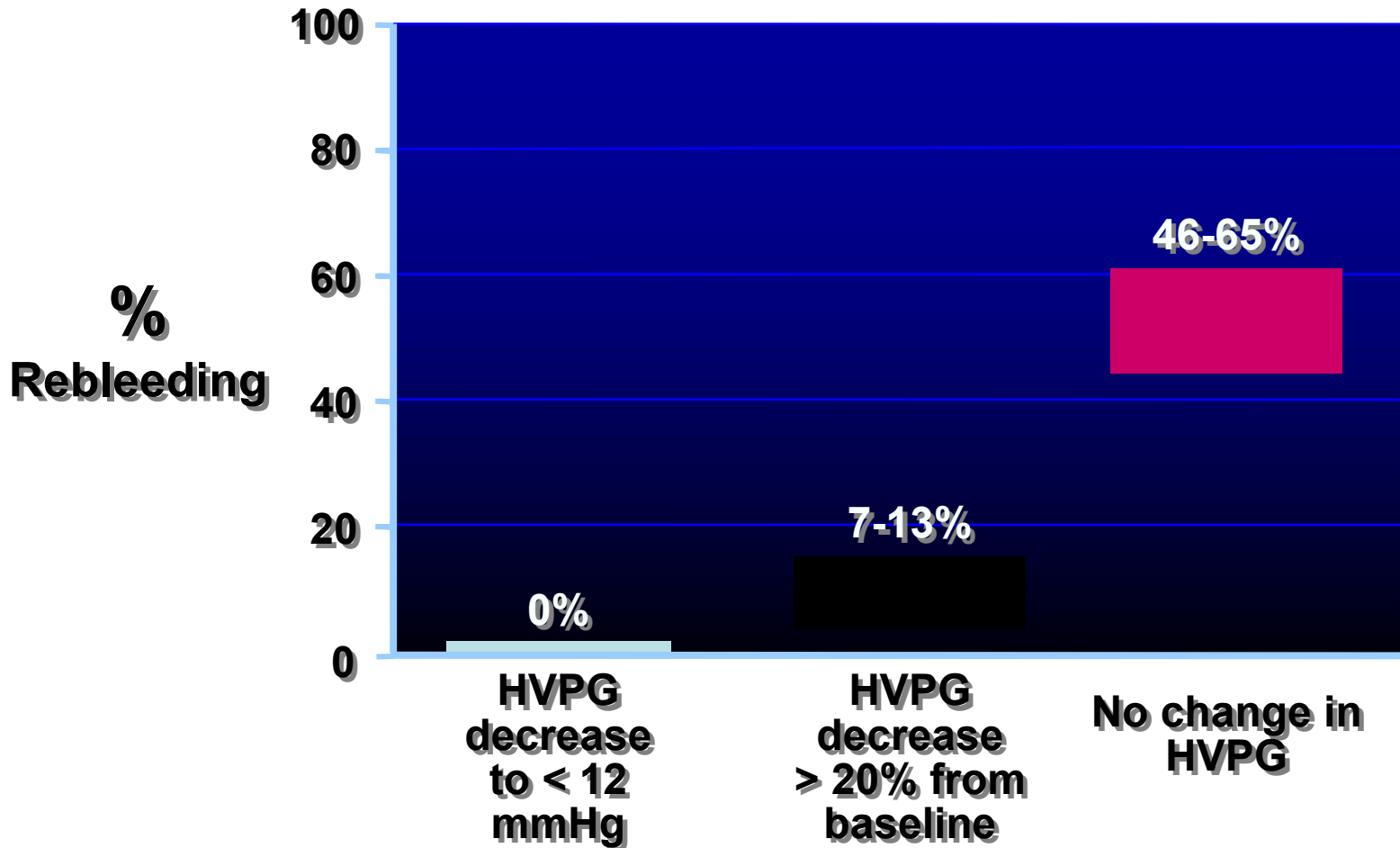
Fig. 1. Kaplan-Meier plot showing cumulative probability of remaining free of variceal rebleeding. Eight-year probability of remaining free of rebleeding was higher in responders than in nonresponders (R, responders; NR, nonresponders).

Risk of first variceal bleeding



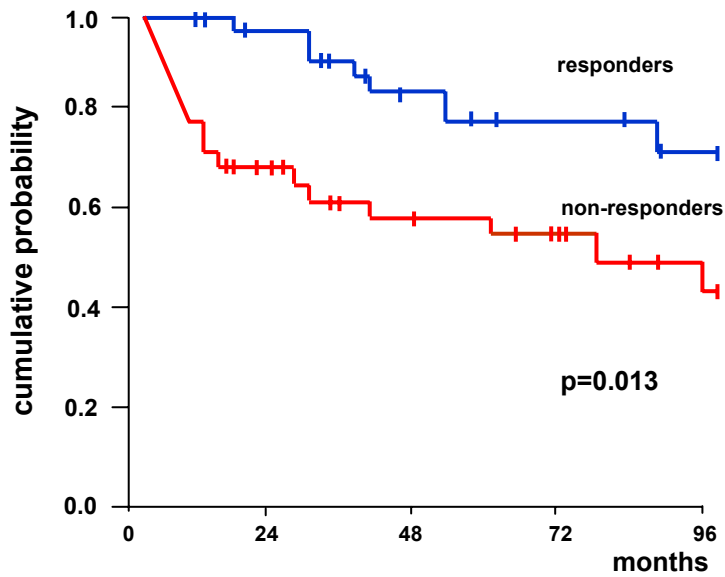
The 8-yr cumulative probability of remaining free of first variceal bleeding was higher in responders than in nonresponders (90% vs 45%, respectively, 95% CI of risk difference: 15-76%, $p=0.026$).

Decrease In Hepatic Venous Pressure Gradient (HVPG) Reduces Risk of Variceal Bleeding

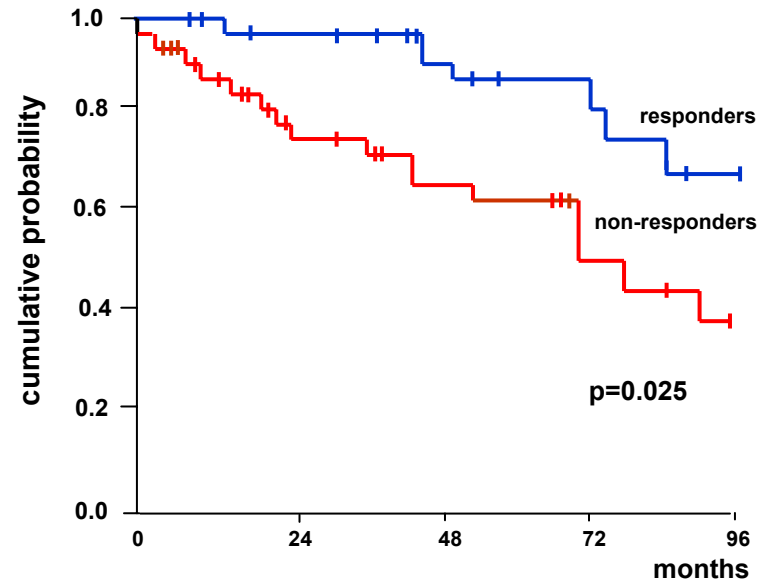


THE EVOLUTION
OF
LIVER DISEASE

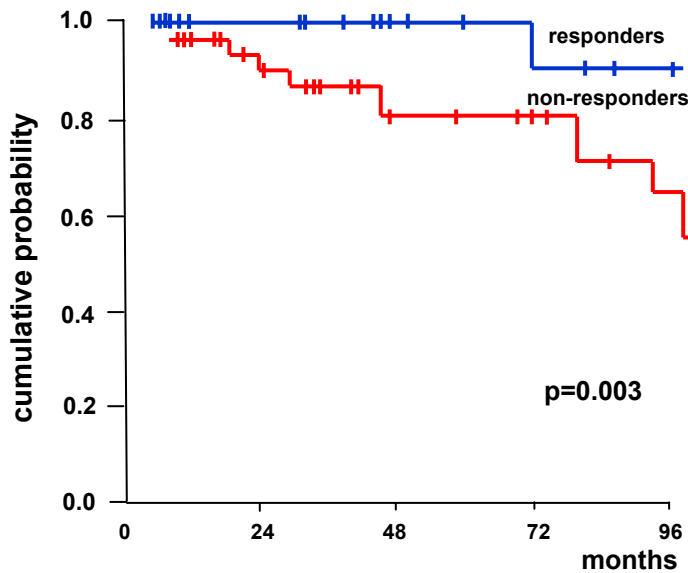
Remaining free of rebleeding



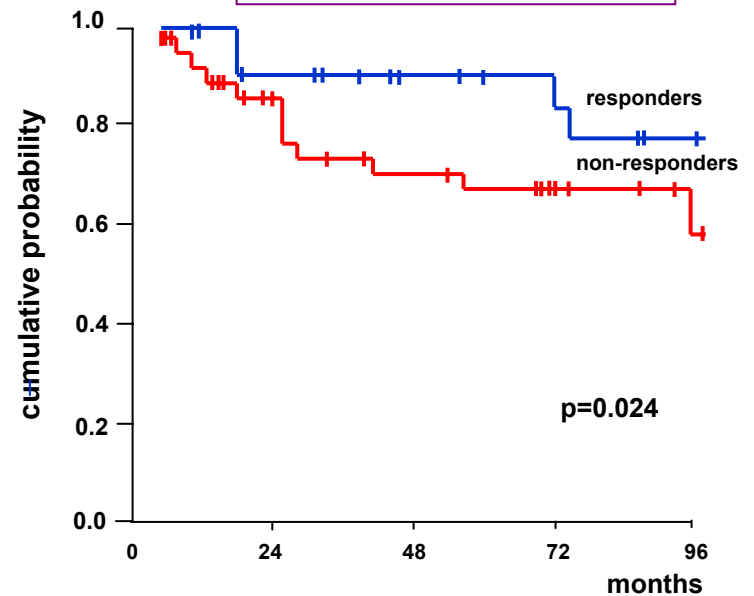
Not reaching ascites



Remaining free of SBP



Remaining free of PSE



HVPG and Response to Antiviral Therapy

- HVPG may be a better surrogate of liver fibrosis in chronic hepatitis

Burroughs AK et al.; Gut 2002

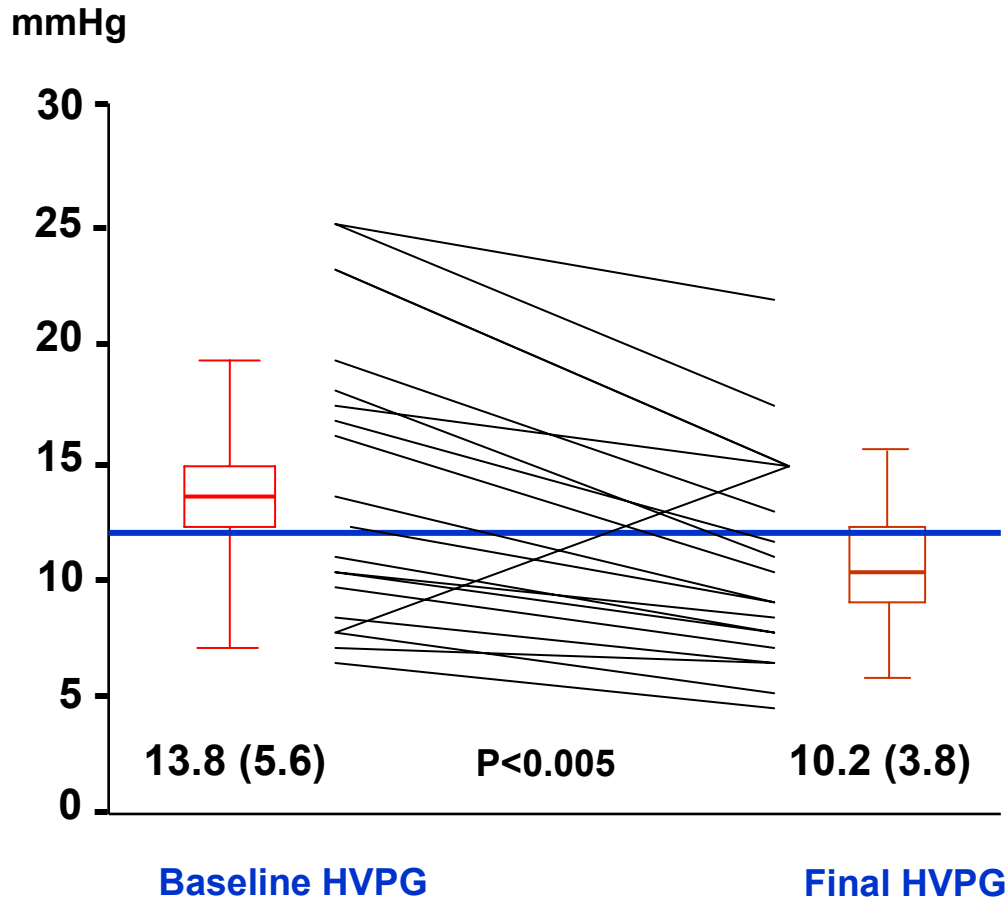
- When HCV recurs after liver transplantation HVPG could be used to select those patients who could benefit from antiviral therapy

Blasco A et al.; Hepatology 2006

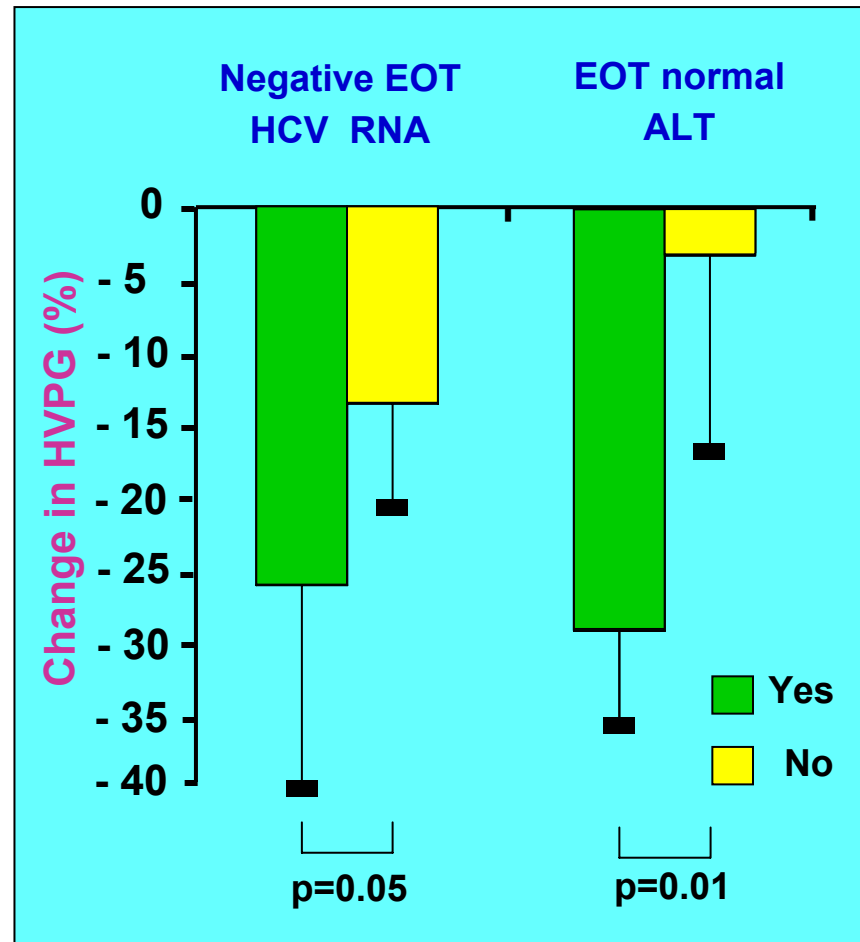
- HVPG may represent a reliable dynamic measurement to monitor progression of chronic liver disease and to assess the response to antiviral therapy

Rincon D et al.; Am J Gastroenterol 2006

Roberts S et al.; Clin Gastroenterol & Hepatol 2007



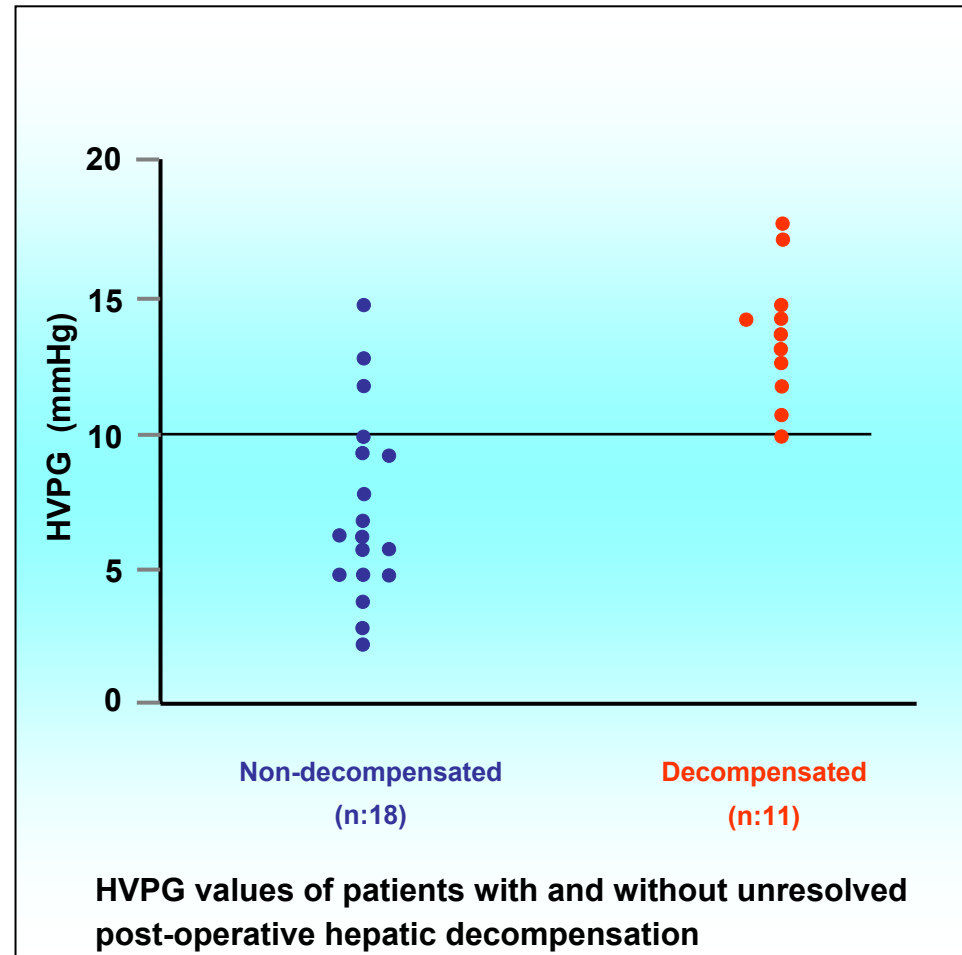
Mean reduction in HVPG: 28.2 (12)%



CANDIDATES FOR
SURGICAL RESECTION
OF HCC

Parameters significantly associated with the development of unresolved postoperative hepatic decompensation

Variable	Decompensated patients	Non-decompensated patients	<i>p</i>
Platelet count ($10^3 / \text{mm}^3$)	82 ± 25	147 ± 74	<0.01
BUN	15 ± 4	20 ± 5	<0.01
Bilirubin (mg/mL)	1.1 ± 0.3	0.7 ± 0.3	<0.02
WHVP (mmHg)	19.5 ± 4.8	12.0 ± 4.9	<0.0004
HVPG (mmHg)	13.9 ± 2.4	7.4 ± 3.4	<0.0001
Hepatic intrinsic clearance (mL/min)	308 ± 144	450 ± 141	<0.02



HVPG and Surgical Resection of HCC

- In compensated cirrhotic patients undergoing surgery for small HCC, HVPG was the only variable independently associated with unresolved decompensation at 3 months

Bruix J et al.; Gastroenterology 1996

- An HVPG <10 mmHg was an independent predictor of survival in Child-Pugh class A cirrhotic patients with resectable HCC

Llovet JM et al.; Hepatology 1999

- Current AASLD guidelines for the management of HCC recommend HVPG measurement in patients with a single lesion who are candidates to liver resection

Bruix J & Sherman M.; Hepatology 2005

AND

WHY TO DO IT

- HVPG measurement has proved to be a safe, convenient and accurate procedure. Practice guidelines are now available in order to give HVPG measurement more reliability
- It provides valuable information for establishing diagnosis, for predicting prognosis and for making therapeutic decisions
- Well established manometric HVPG cut-off values are reliable targets in the therapy of portal hypertension. Therefore, treatments of portal hypertension have well defined reference points and these HVPG reference points should be applied in clinical practice

- Portal pressure measured by the HVPG may be as close as we can come to a validated surrogate outcome in hepatology. Randomised trials of interventions decreasing portal pressure have shown consistent improvement in surrogate outcome and clinical outcomes.

Glud C et al.; J Hepatol 2007