

Traitement Médical et Endoscopique de l'HTP du Cirrhotique

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Traitement de l'HTP chez le cirrhotique

- Diagnostic de l'HTP
- Prophylaxie pré-primaire

I - Prophylaxie primaire

II - Prise en charge et Traitement de l'hémorragie dig. due à l'HTP

III - Prophylaxie secondaire

De Baveno I à Baveno IV

International Workshop on Portal hypertension

- 1990 : Baveno I
- 1995 : Baveno II
- 2000 : Baveno III
- 2005: Baveno IV
- **2010 : Baveno V**



**DIAGNOSTIC de
L'HYPERTENSION PORTALE**

Definition of Clinically Significant Portal Hypertension (CSPH)

- Portal hypertension is defined by an hepatic vein pressure gradient (HVGP) > 5 mmHg.
- CSPH is defined by an increase of HVPG to a threshold ≥ 10 mmHg.
- The presence of varices, variceal hemorrhage and or ascites are complications of portal hypertension.

Screening for CSPH

- All cirrhotic patients should be screened for the presence of varices at the time of initial diagnosis of cirrhosis
- In cirrhotic patients without varices when first seen, endoscopy should be repeated *two yearly* until varices appear unless patient become decompensated
- In compensated patients with small varices, endoscopy should be repeated at *1-2 yearly* to evaluate progression of varices from small into large

Classification des Varices oesophagiennes

Classification internationale ou japonaise (BEPU)

1- Couleur dominante

2- Taille ou grade

3- Siège

4- Signes de la couleur rouge:

zébrures

petits points rouges

gros pts rouges hémato-kystiques

rougeur diffuse

5- Erosions

Facteurs pronostiques

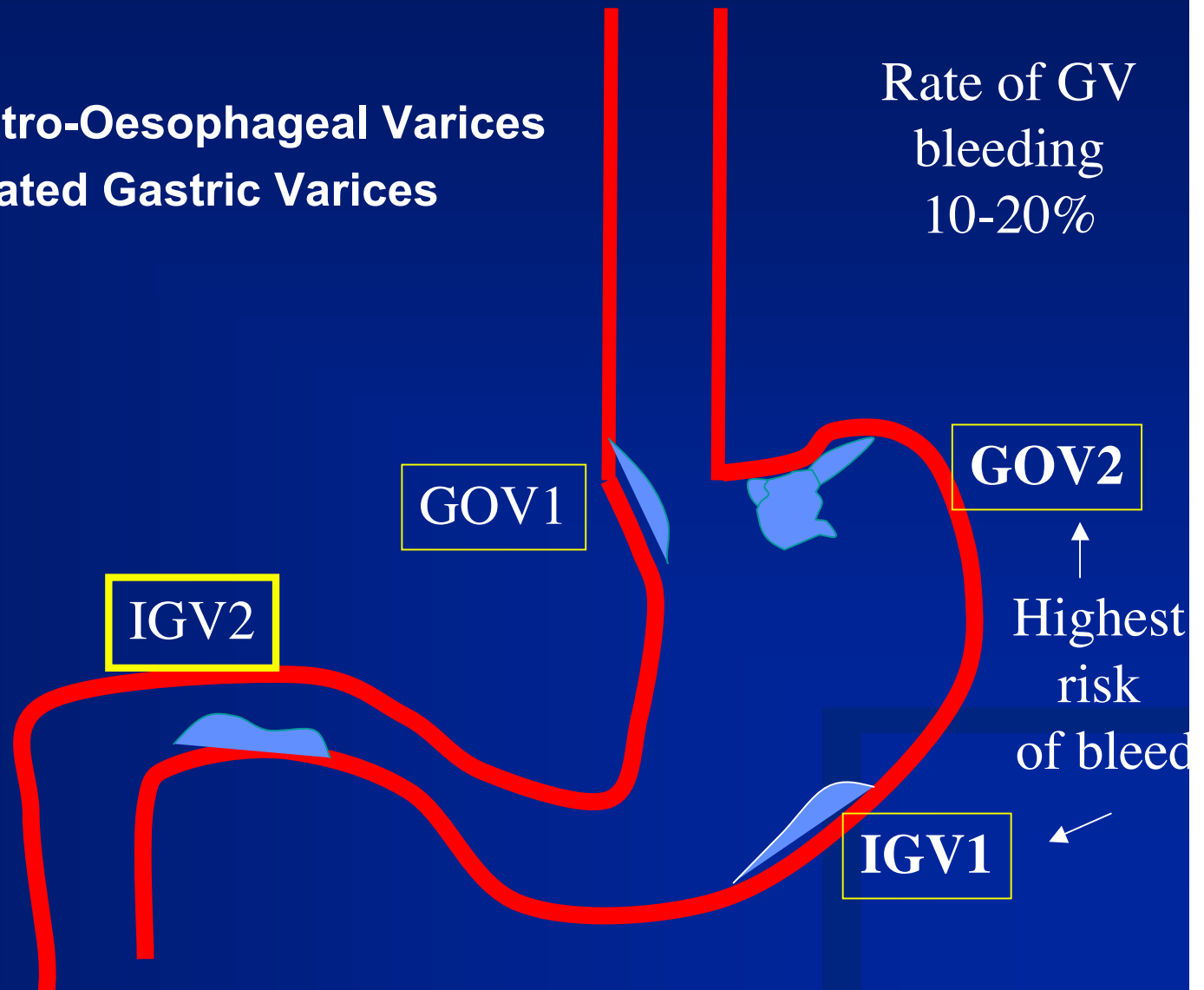
grade II ou III

gros pts rouges hémato-kystiques

Classification of Gastric Varices

- **Gastro-Oesophageal Varices**
- **Isolated Gastric Varices**

Rate of GV
bleeding
10-20%



Incidence and Progression of varices

- Incidence of varices
 - 10-15% / year
- Progression to small varices
 - 5% / year
- Progression from small to large varices
 - 10-15% / year
- **HVGP** is the strongest predictor of the development of varices

Hepatic Vein Pressure Gradient

- HVPG correlates significantly with fibrosis (Sheuer score)
 - Blasco et al, Hepatology 2006, 43(3): 492-9
- HVPG ≥ 10 mmHg is the strongest predictor to develop varices
 - Grossman RJ et al, NEJM 2005; 353: 2254-
- HVPG ≥ 10 mmHg is an independent predictor of decompensation in patients with compensated cirrhosis
- HVPG is an independent predictor of outcome (6/9 studies)
- A decrease of HVPG ≥ 20 % of baseline or HVPG ≤ 12 mmHg after chronic treatment with NSBB are clinically relevant for acute response to NSBB.

Definition of Key Events

Failure to control bleeding (needs to change treatment) if

- Time frame for the acute episode of bleeding should be 5 days.
- One criterion defines failure
 - Fresh hematemesis > 2h after start of specific drug treatment or therapeutic endoscopy. In patients who have a nasogastric, aspiration greater than 100 ml of fresh blood
 - Development of hypovolemic shock
 - 3 gram drop in Hb (= 9% Ht) in those non transfused. The time frame needs to be validated
 - Death.
- Index of blood transfusion requirement (ABRI) ≥ 0.75 at any time point

Adjusted Blood Requirements Index

(Paul Cales proposal)

- **ABRI** = Blood units / (final Ht-initial Ht) + 0.01
 - **ABRI** \geq 0.75
 - 1.9% in controls vs 22.3 % in bleeders
 - 29% in placebo vs 16% in Vapreotide group (p=0.02)

- **Target Hematocrit : 24%**
 - Suggested by 2 RT and one SR.

- Ht every 6h for the first 48 h
- Ht every 12h from D3 to D5

Definition of Key Events

Failure of secondary prophylaxis

- Failure to prevent rebleeding is defined as a single episode of clinically significant rebleeding from portal hypertensive sources after day 5 (5;D).
- Clinically significant rebleeding:
 - Recurrent melena or hematemesis resulting in any of the following:
 - hospital admission
 - blood transfusion
 - 3 g drop in Hb
 - death within 6 weeks

Pre-primary prophylaxis

Pre-primary prophylaxis

Prevention of appearing of varices

- Pre-primary prophylaxis should only include patients without gastro-oesophageal varices. (5;D)
- Treatment of underlying liver disease may reduce portal hypertension and prevent its clinical complications. (1b;A)
- HVPG > 10 mmHg is predictive of varices formation and decompensation (1;A)
- HVPG measurement in pre-primary prophylaxis may be recommended only the context of clinical trials. (5;D)
- There is no indication, at this time, to use beta-blockers to prevent the formation of varices. (1b;A)

Prévention pré-primaire : Absence d'intérêt des β -bloquants

**Étude randomisée en double aveugle (timolol vs placebo)
Résultats en intention de traiter
Patients avec hypertension portale sans varice**

	Timolol (n = 108)	Placebo (n = 105)	p
Apparition des varices	42	42	NS
Décès ou TH	17	17	NS
Evènements Indésirables	20	6	< 0,01

**Traitement prophylactique de la survenue du
premier épisode hémorragique**

PROPHYLAXIE PRIMAIRE

Traitement prophylactique de la survenue du premier épisode hémorragique

- 2/3 des patients présentent un hémorragie dans l'année qui suit le diagnostic des VO.
- Mortalité du premier épisode d'Hémorragie Digestive est de 20 %
- **Facteurs prédictifs de saignement:**
 - taille des varices +++
 - Signes de la lignée rouge (vésicule hématokystique)
 - Gravité cirrhose ++

Prévention de la progression des varices

Prophylaxie primaire :

Étude randomisée contrôlée (nadolol vs placebo)

Résultats en intention de traiter

Patients avec varices œsophagiennes de petite taille

	Nadolol (n = 83)	Placebo (n = 78)	p
Aggravation des varices	9	29	< 0,01
Décès ou TH	28	36	NS
Evènements Indésirables	9	1	0,02

Traitement prophylactique de la survenue du premier épisode hémorragique

β -Bloquants vs Contrôle

10 études contrôlés randomisés (1037 malades)

8 études: Avlocardyl VO grade II et III

2 études : Nadolol

Hémorragie : 4 études S, 1 étude S contre β -bloquants, 5 NS

Mortalité: 1 étude S, 9 NS

	β -bloquants	Contrôle	p
Hémorragie:	15%	25%	< 0,001
Mortalité:	24%	27%	NS

Traitement prophylactique de la survenue du premier épisode hémorragique

Sclérothérapie vs Contrôle

21 études contrôlées randomisées (1820 malades)

Hémorragie : 7 études S, 1 étude S contre sclérose, 13 NS

Mortalité: 5 études S, 1 étude S contre sclérose, 15 NS

	Sclérothérapie	Contrôle	p
Hémorragie:	24%	35%	< 0,001
Mortalité:	30%	37%	< 0,01

Traitement prophylactique de la survenue du premier épisode hémorragique

Shunt porto-cave vs Contrôle

4 études contrôlées randomisées (285 malades)

Hémorragie : 2 études S, 2 NS

Mortalité: 4 études NS

	Shunt	Contrôle	p
Hémorragie:	9%	26%	< 0,001
Mortalité:	53%	40%	< 0,05

Traitement prophylactique de la survenue du premier épisode hémorragique

β - bloquants vs Sclérothérapie

2 études contrôlées randomisées (226 malades)

Hémorragie : 1 étude S, 1NS

Mortalité: 2 études NS

	β -bloquants	Sclérose	p
Hémorragie:	13%	19%	NS
Mortalité:	21%	31%	NS

Prevention of the first bleeding episode

Patients with **small varices**

- Patients with small varices with red wale marks or Child C class have an increased risk of bleeding (1b;A) and should be treated with nonselective beta blockers (NSBB) (5;D)
- Patients with small varices without signs of increased risk may be treated with NSBB to prevent progression of varices and bleeding. (1b;A)
- Further studies are required to confirm their benefit.

Prevention of the first bleeding episode

- Non selective β -blockers reduce the risk of first variceal bleeding by 45%
- **β -blockers** in general are given according to the maximum tolerated dose (320 mg for propranolol and 240 mg for Nadolol), but heart rate not lower than 55-60 b/mn
- Most experts consider that any drug that **reduces HVPG by >20%** is effective although it is conceivable that drugs may act in different ways that cannot be evaluated by measurement of HVPG
 - Some experts consider that reduction of HVPG by 10 or 15% is effective

Prophylaxie primaire

Ligature à l'élastique vs Placebo

- Méta-analyse (5 études randomisées, 601 patients):
- En faveur de la ligature à l'élastique
 - Risque hémorragique : RR : 0.36 (0.26-0.50); NNT : 4.1
 - Mortalité par hémorragie : RR 0.20 (0.11-0.39); NNT : 6.7
 - Mortalité globale : RR : 0.55 (0.43-0.71); NNT : 5.3

Prophylaxie primaire

Ligature vs β -bloquants

Méta-analyse : 7 études randomisées

■ Risque hémorragique :

■ β -bloquants : 65/278 : 23%

■ Ligature : 38/276 : 14%

■ En faveur de la ligature RR : 0,64 (0,40-1,01)

En incluant toutes les études + Abstracts):

■ En faveur de la ligature RR : 0,63 (0,46-0,87)

■ Pas de différence en terme de survie RR : 0,98

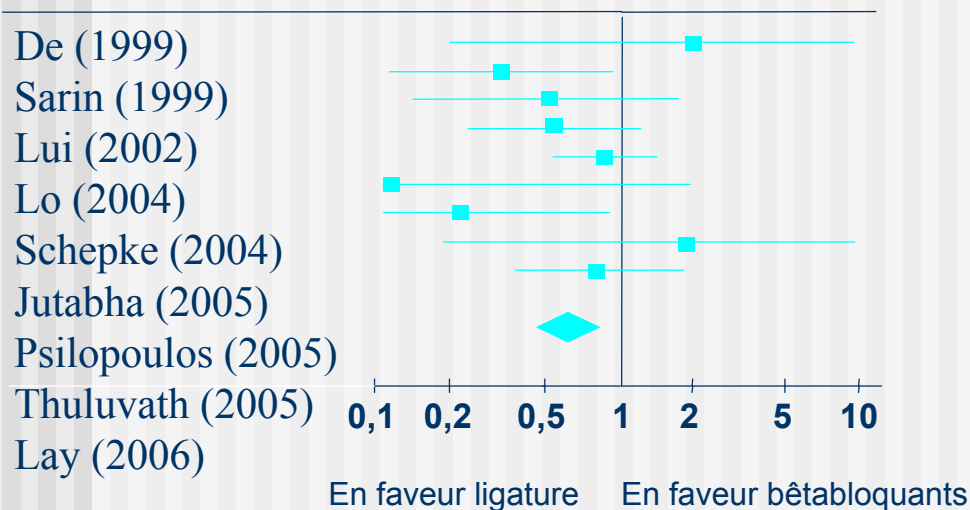
■ Pas de bénéfice si **combinaison β -bloquants + ligature vs ligature** (1 étude randomisée)

Prophylaxie primaire : ligature de VO versus bêtabloquants

Une méta-analyse : 9 études ayant inclus 734 patients

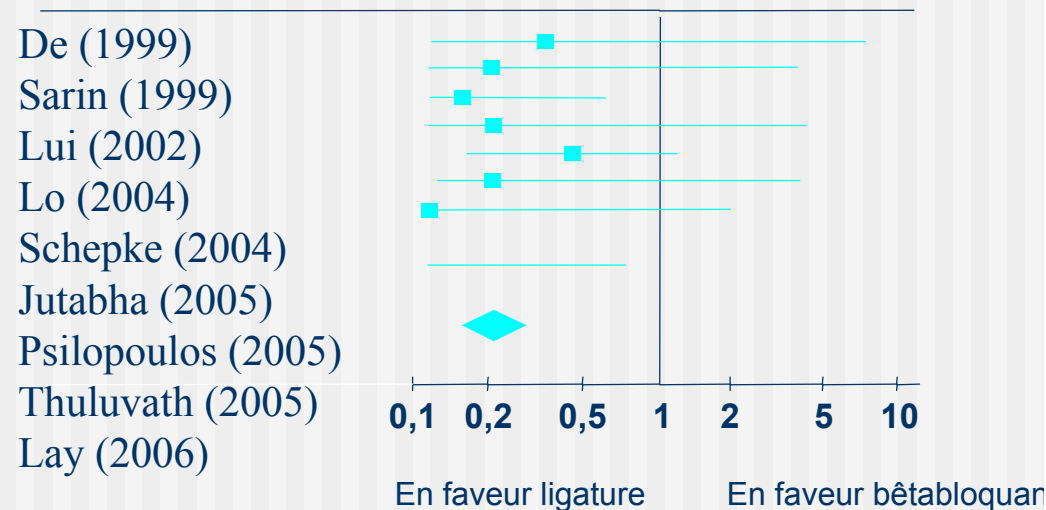
Prévention hémorragique

RR (fixed)
IC₉₅



Effets indésirables

RR (fixed)
IC₉₅



Pas de différence significative en termes de survie globale

- **En prophylaxie primaire, par rapport aux bêtabloquants, la ligature de VO diminue le pourcentage de rupture de VO et entraîne moins d'effets indésirables**
- **À l'inverse, elle n'améliore pas la survie globale**

Primary prophylaxis

medium and large varices (1)

- Either NSBB or endoscopic band ligation (EBL) is recommended for the prevention of first variceal bleeding of medium or large varices. (1a; A)
- Choice of treatment should be based on local resources and expertise, patient preference and characteristics, side effects and contraindications. (5;D)
- Carvedilol is a promising alternative (1b;A) which needs to be further explored.
- Shunt therapy, endoscopic sclerotherapy and IMN **should not be used** in the first variceal bleeding prophylaxis.

Primary prophylaxis

medium and large varices (2)

- There is insufficient data to recommend the use of NSBB in combination with Isosorbide-5- Mononitrate (ISMN), spironolactone, or EBL for primary prophylaxis. (1b;A)
- Patients with gastric varices may be treated with NSBB

Primary prophylaxis (HVGP)

- In centers where adequate resources and expertise are available, HVPG measurements should be routinely used for prognostic and therapeutic indications. (5;D)
- Controlled trials using pharmacological therapy in primary prophylaxis should include HVPG measurements. (5;D)
- A decrease in HVPG of at least 20% from baseline or to ≤ 12 mmHg after chronic treatment with NSBB is clinically relevant in the setting of primary prophylaxis. (1a; A)
- Acute HVPG response to intravenous propranolol may be used to identify responders to beta-blockers, specifically a decrease in HVPG of 10% or to < 12 mmHg may be relevant in this setting (1b; A)

Traitement prophylactique de la survenue du premier épisode hémorragique

Ligature : +++++

β -Bloquants: +++

Sclérose: +

Chirurgie: NON

Traitement de l'hémorragie digestive de l'HTP



Rupture de VO ou V. Gastriques

Diagnostic

Cause la plus fréquente HTP (95%) = Cirrhose

Evaluer la gravité de la cirrhose :

Classification de Child, Child-Pugh, ou Paul Brousse

Faire le diagnostic : Endoscopie

Rupture de varices (50- 60%)

saignement en jet

caillot adhérent , téton blanc sur une varice

VO sans aucune autre lésion

Erosions gastro-duodénales aiguës (20 - 30%)

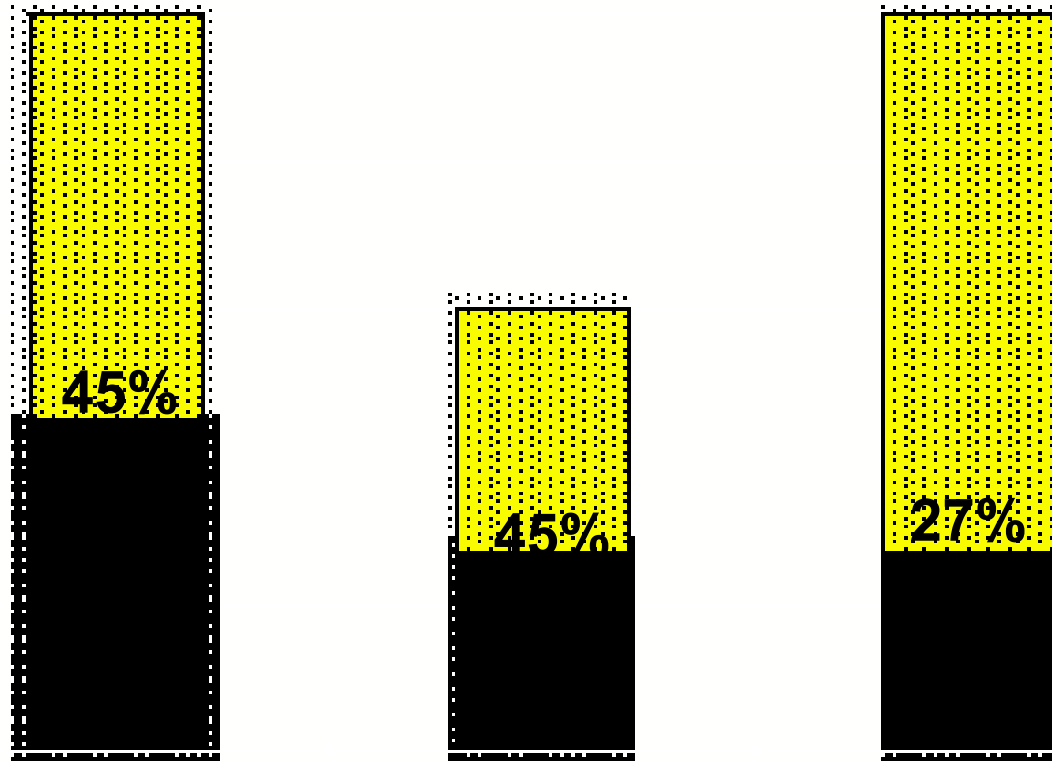
Ulcère gastro-duodéal (5- 10%)

Principes de Réanimation

- Evaluation de la gravité de l'hémorragie
 - **Pouls, TA**
 - Hypotension orthostatique
 - Tachycardie avec vasoconstriction
 - Signes de choc
 - **Micro-hématocrite, hématocrite, Hémoglobine**

Hématocrite avant et après Hémorragie digestive

Volume
(litres)



Hémorragie

Hémorragie

Hémorragie

Principes de reanimation (2)

- **Les premiers gestes:**
 - A : Liberté des voies aériennes
 - B : Oxygénation
 - C: Circulation: 2 voies veineuses périphériques (Désilet fémoral ou cathéter central)
 - ± Sonde urinaire
- **Bilan sanguin initial:**
 - Groupe sanguin, RAI
 - NFS, plaquettes, coagulation
 - Constantes métaboliques et biologie hépatique

Principes de reanimation (3)

- **Remplissage vasculaire:**
 - Les colloïdes:
 - Les gélatines fluides: Plasmion
 - Les dextrans: Rhéomacrodex
 - Les dérivés de l'amidon: Voluven
 - Les cristalloïdes:
 - Ringer lactate, Bicarbonates
 - Les produits sanguins et dérivés:
 - Sérum albumine 4% et 20%
 - Culots globulaires
 - Plasma solvant détergent (PSD) ou Plasma viro atténué (PVA) : 1 unité pour 2-3 culots globulaires
 - Plaquettes
- **Maintenir un hématoците 25-30%**

Principes de reanimation (4)

- **Préparation de l'endoscopie**

- Sonde naso-gastrique:

- Lavage gastrique à l'eau glacé:

- Reflet direct de la poursuite du saignement
- Diminution du flux sanguin pariétal (vasoconstriction)
- Risque d'hypothermie et troubles de la coagulation
- Préparation pour l'endoscopie

- **Erythromycine en IV**

- Quantification de la gravité de l'hémorragie

- Retentissement hémodynamique
- Retentissement hématologique
- La persistance du saignement (par le lavage gastrique)
- Les transfusions sanguines+++

Facteurs de gravité de l'hémorragie

- Etat de choc
- L'acidose métabolique, Lactatémie
- L'administration de drogues inotropes
- Transfusions > 6 culots globulaires
- Récidive précoce de l'hémorragie

- Facteurs associés:
 - Age > 60 ans
 - Insuffisance viscérale majeure
 - Type de l'hémorragie (haute >>> basse)
 - Siège inconnu ++ (surtout avant intervention)

Treating of the acute bleeding episode

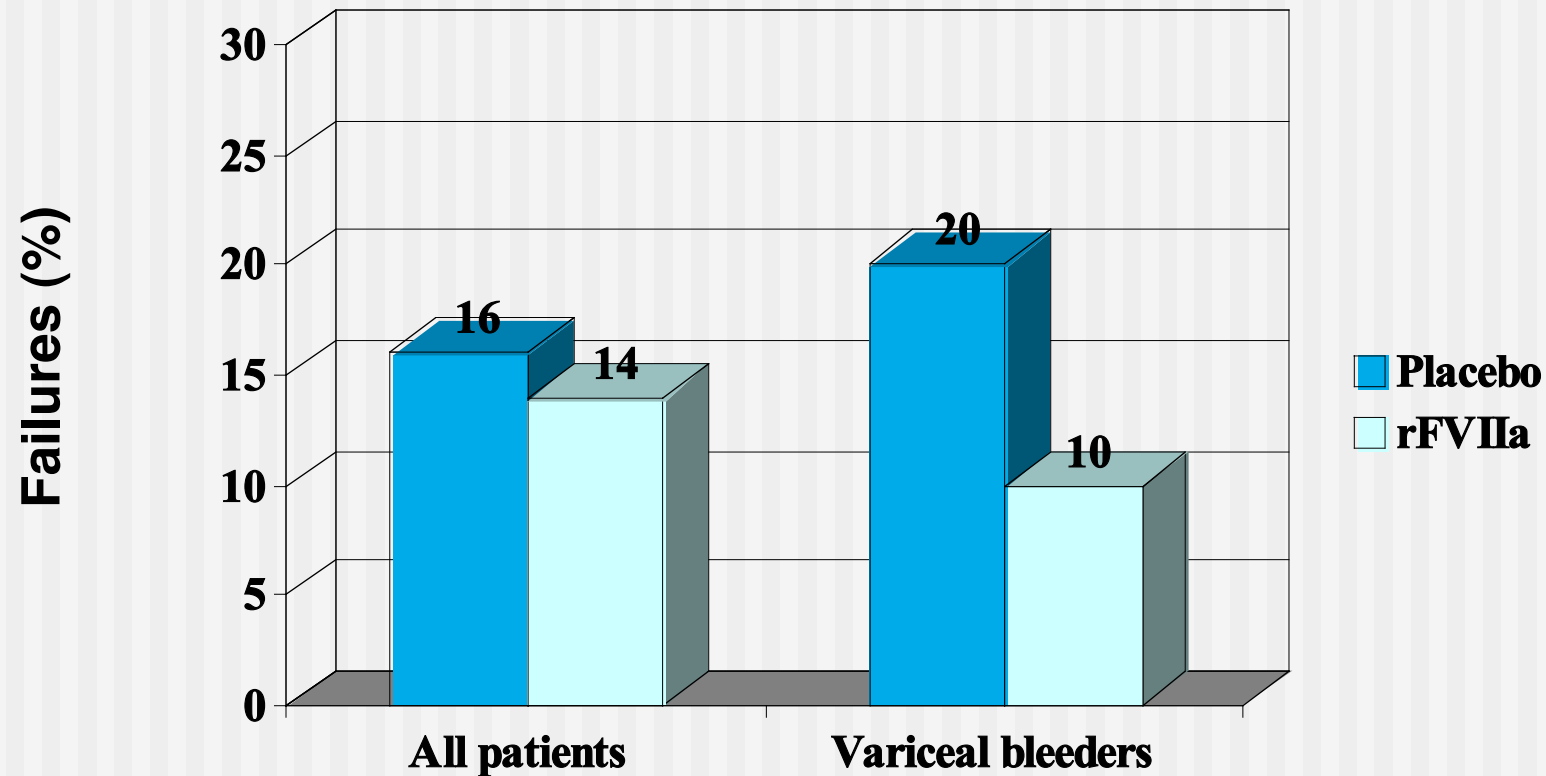
- **Blood volume restitution** should be done conservatively, using Plasma expanders to maintain hemodynamic stability
- PRBC to maintain the Hb at approximately 7-8g/dl depending on other factors such as patients comorbidities, age, hemodynamic status and presence of ongoing bleeding clinically.

Treating of the acute bleeding episode

Coagulation disorders :

- Recommendations regarding management of coagulopathy and thrombocytopenia cannot be made on the basis of currently available data (5:D)
- PT/INR is not a reliable indicator of the coagulation status in patients with cirrhosis (1b; A)

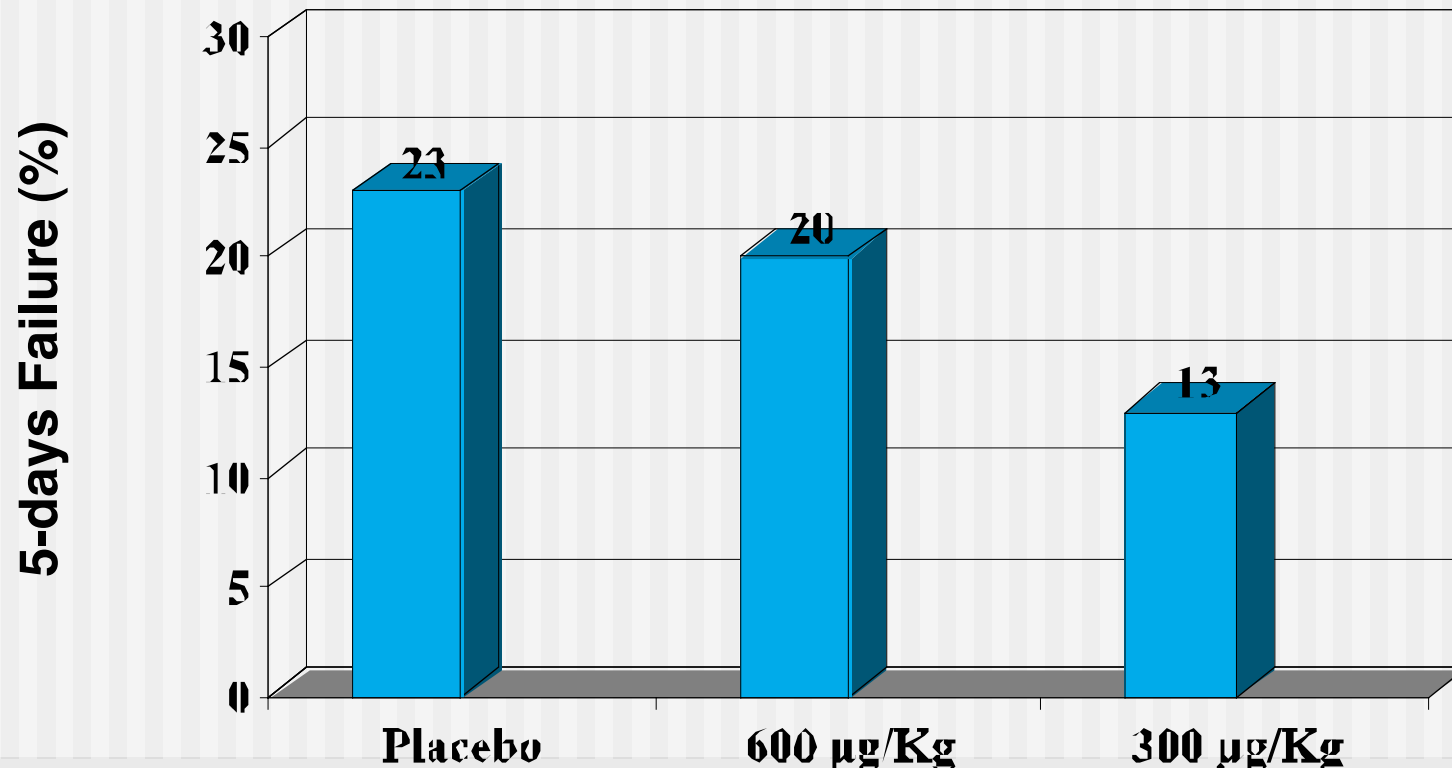
Recombinant FVII in Upper GI bleeding



Recombinant FVII in Acute variceal bleeding in advanced cirrhosis (1)

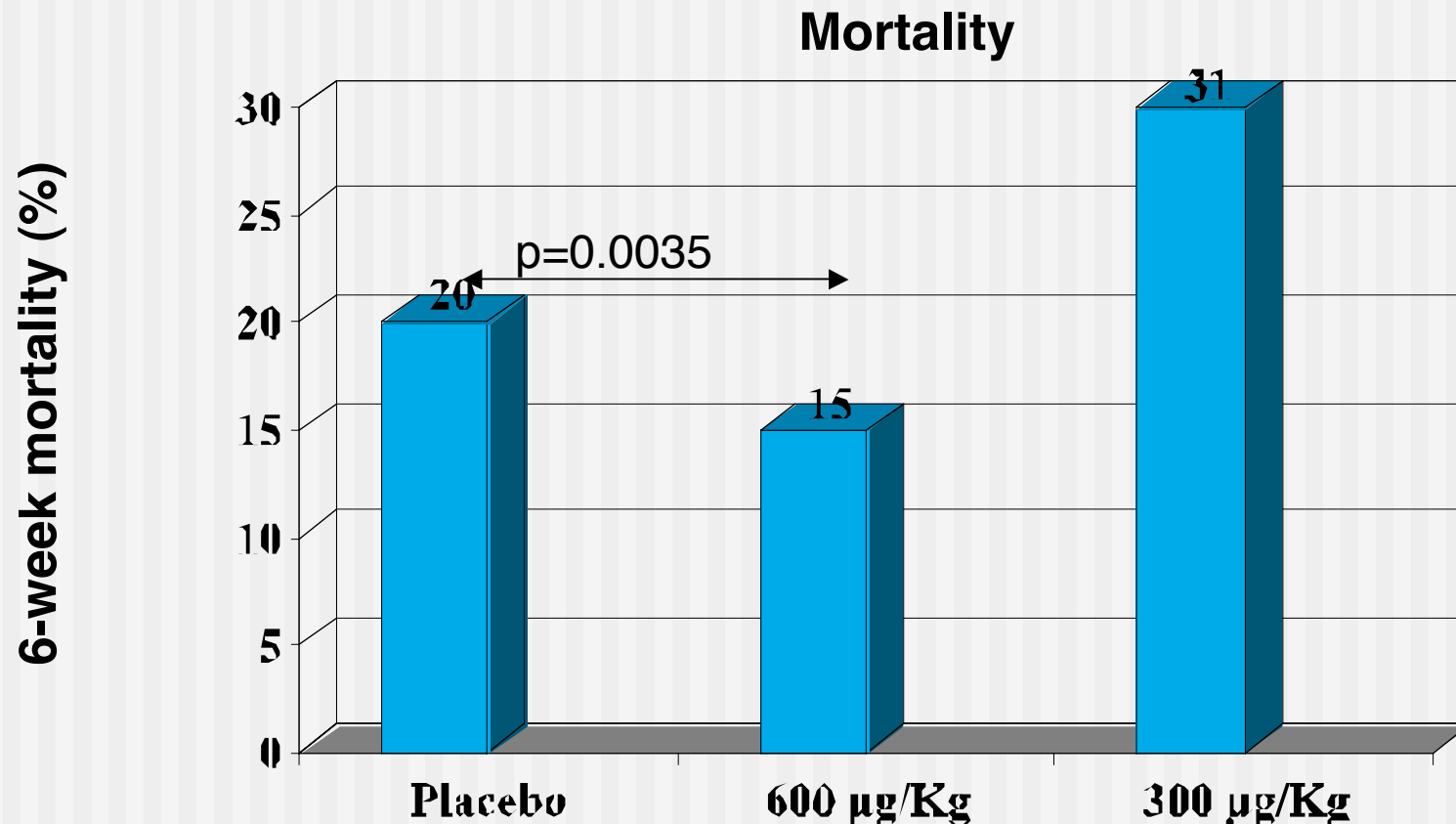
256 patients with Cirrhosis (Child-Pugh C) and Active Variceal bleeding at time of endoscopy

**Primary end-point
Failure to control bleeding at day-5**



Recombinant FVII in Acute variceal bleeding in advanced cirrhosis (2)

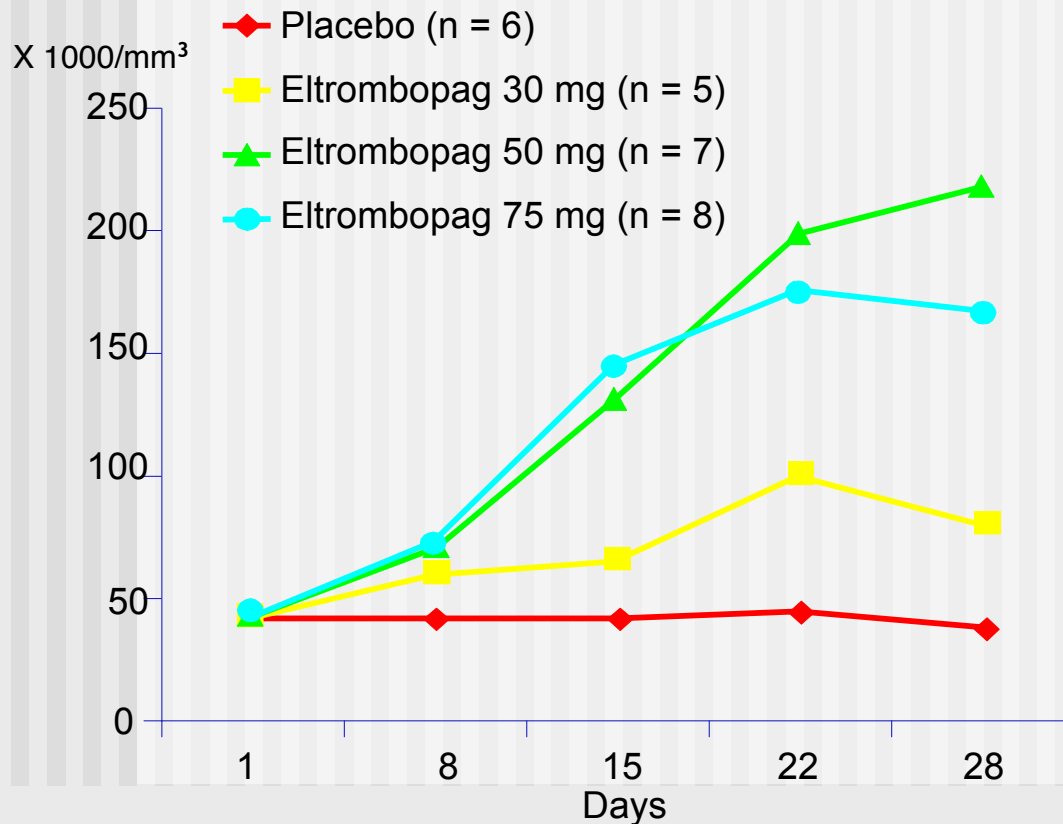
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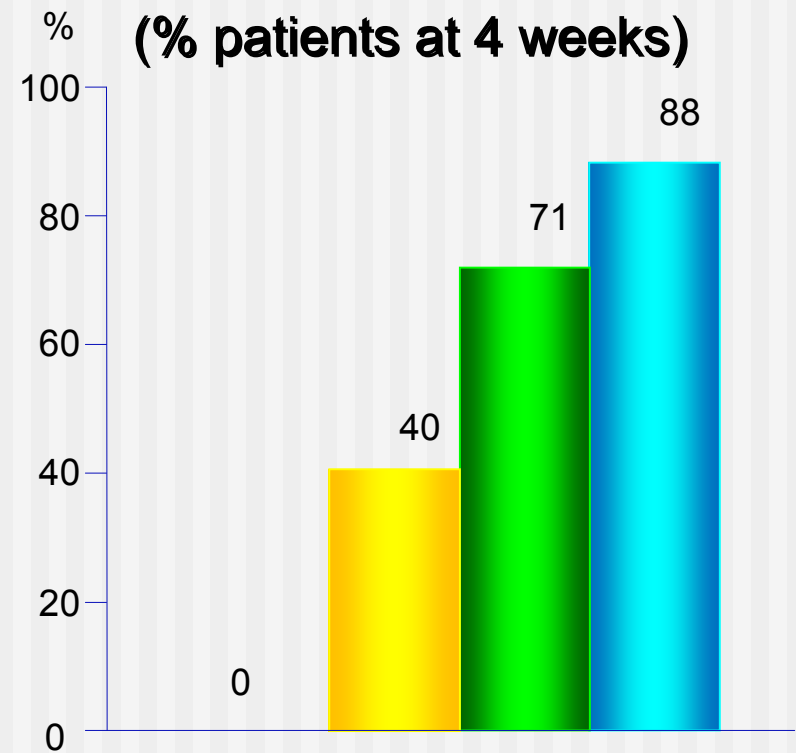
Eltrombopag : correct thrombocytopenia in cirrhotic patients

- A randomized double blind study (sub-group)
- Patients with HCV cirrhosis and platelets $<50\ 000 /\text{mm}^3$ (n= 26)

Platelets count (median)



**Platelets $> 100\ 000/\text{mm}^3$
(% patients at 4 weeks)**



Erythromycine Infusion prior to Endoscopy in patients with Upper GI bleeding

Author	Treatment	N° of Patients/ patients with cirrhosis	Empty stomach	Need for second look endoscopy
Frossard JL et al	Erythromycin (E)	51/13	82% *	12% *
	Placebo (P)	54/19	33%	31%
Coffin B et al	E + Gastric lavage	19/4	90% *	16%
	Gastric lavage	22/9	55%	45%
Carbonnel N et al	E + Gastric lavage	49/32	70% *	24%
	P + Gastric lavage	50/33	48%	24%

Frossard JL, *Gastro* 1992; 123:17. Coffin B, *Gastro Endosc* 2002; 56:174.
Carbonell N, *Am J Gastro* 20006; 101:1211-5

* p < 0.05

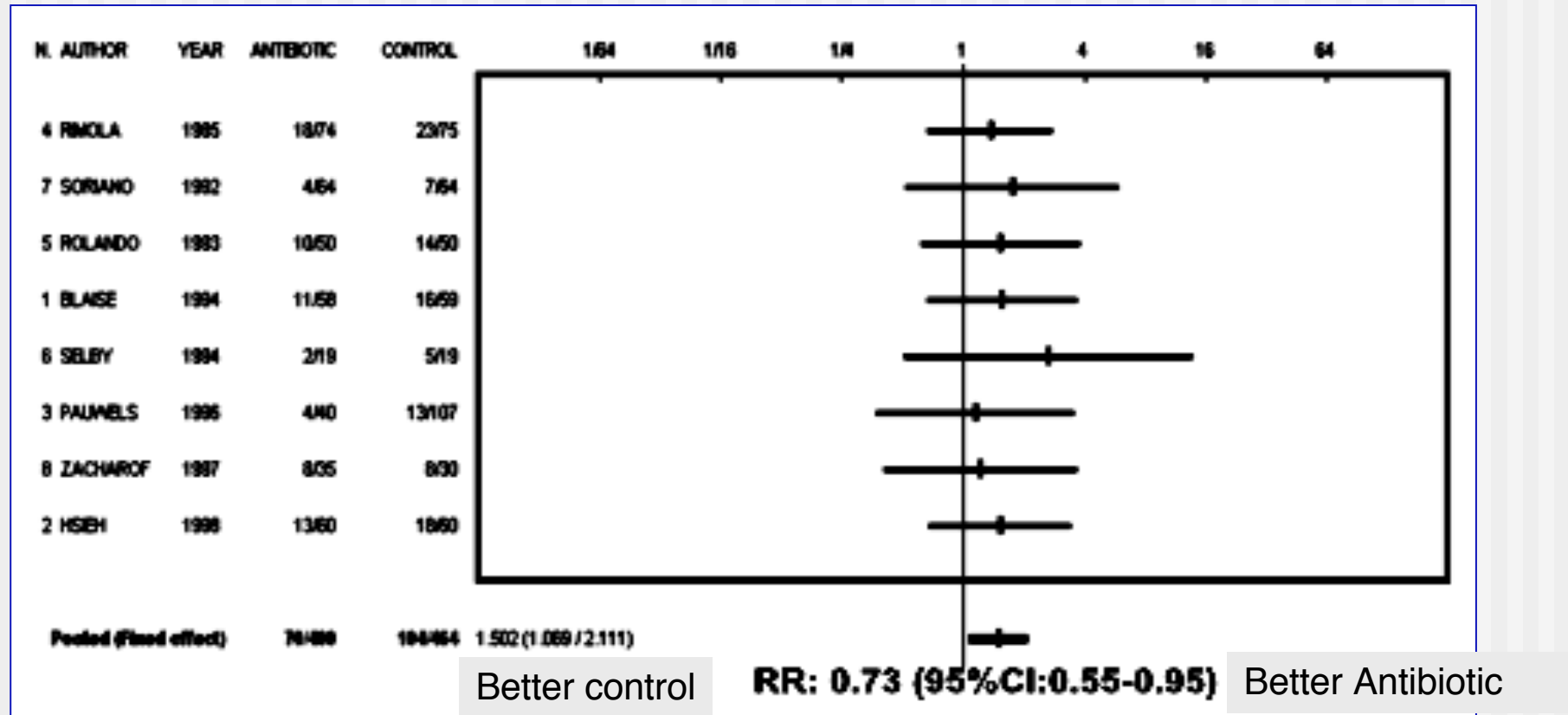
Treating of the acute bleeding episode

Antibioprophylaxis

- The presence of infection should be considered in all patients
- Antibiotic prophylaxis is an integral part of therapy for patients presenting with variceal bleeding and should be instituted from admission (1a;A)
- Oral quinolones are recommended for most patients (1b;A)
- IV ceftriaxone should be considered in patients with advanced cirrhosis or quinolone resistance or previous quinolone prophylaxis (5;D)

Antibioprophylaxis reduce Mortality

Metaanalysis : 8 Randomized trials: 864 patients



- Reduction of incidence of bacterial infections: RR 0.40 (95%CI: 0.32-0.51)

*Trials showed no significant heterogeneity

Antibioprophylaxis : Which Antibiotics ?

- [Blaise 1994](#): IV/oral ofloxacin + amoxicillin/clavulanic acid versus no antibiotic
- [Gulberg 1999](#): ceftriaxone (low dose, 1g) versus IV ceftriaxone (high dose, 2g)
- [Hsieh 1998](#): oral ciprofloxacin versus placebo
- [Pauwels 1996](#): IV/oral ciprofloxacin + amoxicillin/clavulanic acid versus no antibiotic
- [Rimola 1985](#): non-absorbable antibiotics (oral gentamicin, vancomycin, and nystatin; or oral neomycin, colistin, and nystatin) versus no antibiotic
- [Rolando 1993](#): imipenem + cilastin versus dextrose-saline solution
- [Sabat 1998](#): ceftriaxone + oral norfloxacin versus oral norfloxacin
- [Selby 1994](#): cefotaxime versus no antibiotic prophylaxis;
- [Soriano 1992](#): oral norfloxacin versus no antibiotic
- [Spanish Group 1998](#): oral norfloxacin versus oral ofloxacin
- [Zacharof 1997](#): oral ciprofloxacin versus no antibiotic

*** Treatment durations varied from one single dose up to ten days.**

Treating of the acute bleeding episode

Preventing hepatic encephalopathy

- Recommendations regarding management and prevention of encephalopathy in patients with cirrhosis and upper GI bleeding cannot be made on the basis of currently available data

(5; D)

Treating of the acute bleeding episode

Assessment to Prognosis

- HPVG > 20 mmHg, Child-Pugh class C and active bleeding at endoscopy, most consistently found to predict 5-day treatment failure. (2b;B)
- Child-Pugh class C, MELD score > 18 , and failure to control bleeding or early rebleeding are the variables most consistently found to predict 6-week mortality. (2b;B)

Bleeding from varices in cirrhotic patients.

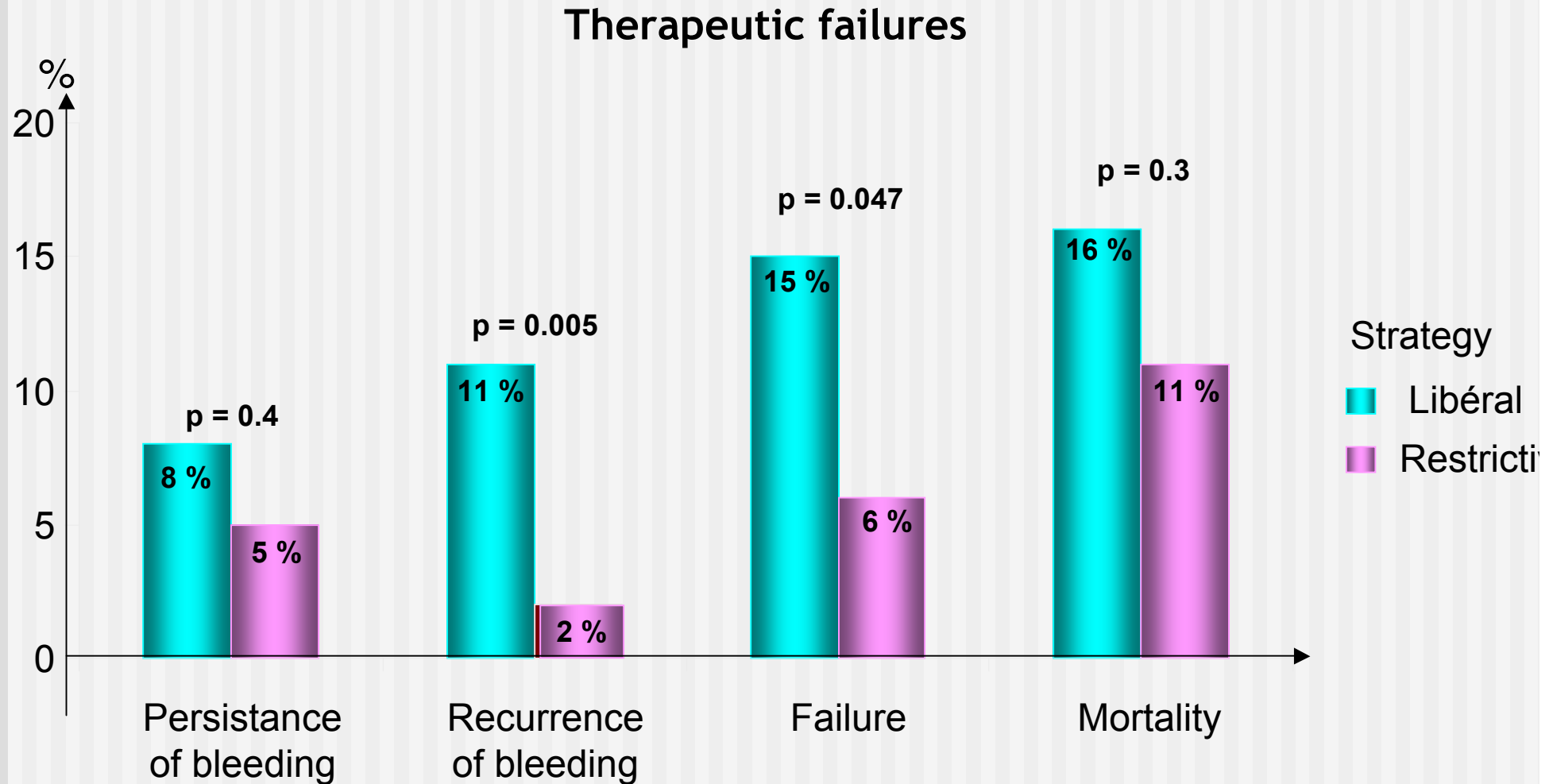
When to Transfuse ? (1)

A prospective study: 601 cirrhotic patients with UGI bleeding (2003-2008)
242 were related to PHT and 214 were randomized

- Treatment : somatostatine + PPI + antibioprophylaxis + endoscopy
- Randomization according to the transfusion strategy :
 - Free (n = 105) : level of hemoglobin = 9 g/dl , aim = 9 – 10 g/dl
 - Restrictive (n = 109) : level of hemoglobin = 7 g/dl, aim = 7 – 8 g/dl

	Liberal Strategy (n = 105)	Restrictive Strategy (n = 109)	p
Transfusion (Blood units)	4.9 ± 4.9	1.9 ± 2.5	< 0.001
Patients not transfused	9%	38%	< 0.001
Hemoglobin at discharge (g/dl)	10.1 ± 1.6	9.2 ± 1.9	< 0.001

Bleeding from varices in cirrhotic patients. When to Transfuse ? (2)



Failure of endoscopic control of Variceal bleeding within 5 days

- Not more than two endoscopic treatment
- If massive bleeding one is enough
 - Naso-gastric tube
 - 50% Yes
 - 50% No

Rupture de VO ou V. Gastriques Sondes de Tamponnement

- Sonde de Blakemore :

ballonnet gastrique 300 ml d'air

ballonnet oesophagien 40-60 ml d'air (VO ou VG)

- Sonde de Linton/ Michel :

ballonnet gastrique 600 ml d'air (VG)

Légère traction

Ablation après 48 heures

Blakemore > Linton

- Hémostase : 70-90%
- Récidive hémorragique : 40 - 50%
- Complications : 14% (pneumopathies, ulcérations)

Indications :

Hémorragie cataclysmique

Treating of the acute bleeding episode

Use of ballon tamponade :

- Balloon tamponade should only be used in massive bleeding as a temporary « bridge » until definitive treatment can be instituted for a maximum 24h and inserted preferably in an intensive care facility. (5;D)

Rupture de VO ou V. Gastriques

Traitement Pharmacologique

- **Vasopressine** : (0,4 U / mn) en perfusion continue
 - vasoconstricteur puissant,
 - Accidents ischémiques sévères, CI chez les cardiaques
- **Vasopressine + dérivés nitrés**
- **Terlipressine** (Glypressine®) :
 - 1- 2 mg IVD/4-6H en fonction du poids
- **Somatostatine** (Somatostatine UCB®, Modustatine®) :
 - 250 µg/h en bolus puis 250 µg/h en continue
- **Octreotide** (Sandostatine®) :
 - 25 µg/h en continue
- **Vapreotide**

Treating of the acute bleeding episode

Pharmacological treatment

- In suspected variceal bleeding, vasoactive drugs should be started as soon as possible prior to endoscopy (1b; A)
- Vasoactive drugs (terlipressin, somatostatin, octreotide, vapreotide) therapy should be used in combination therapy and continued to up 5 days (1a; A)

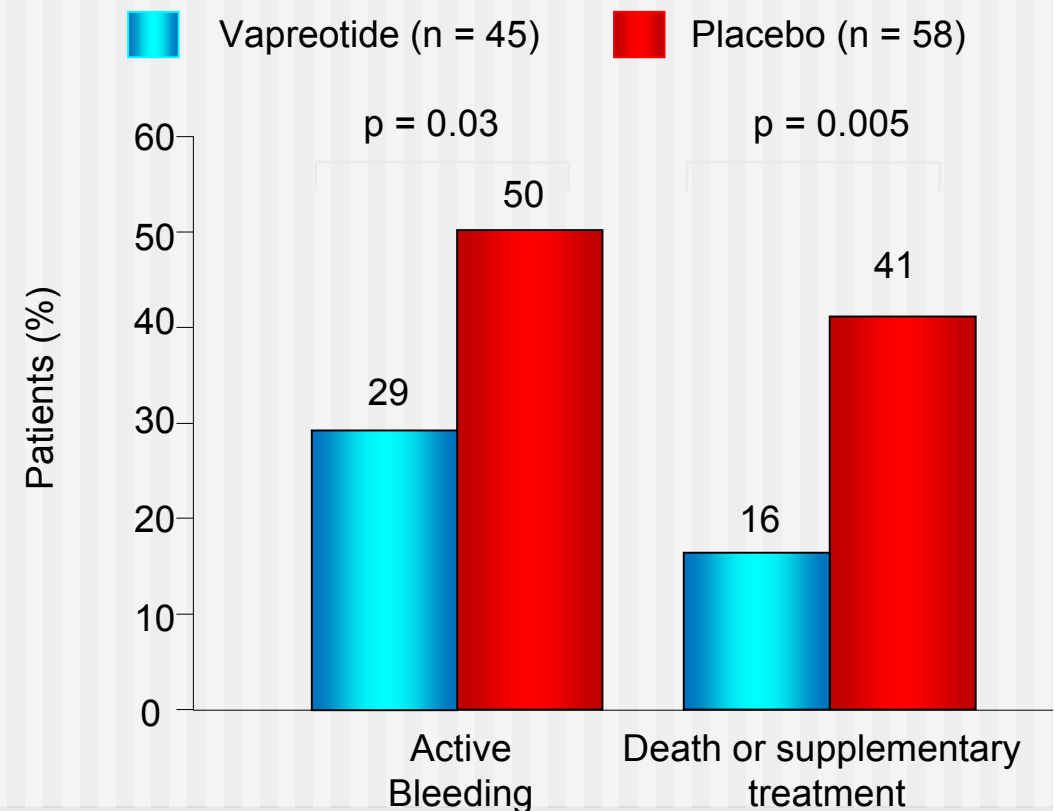
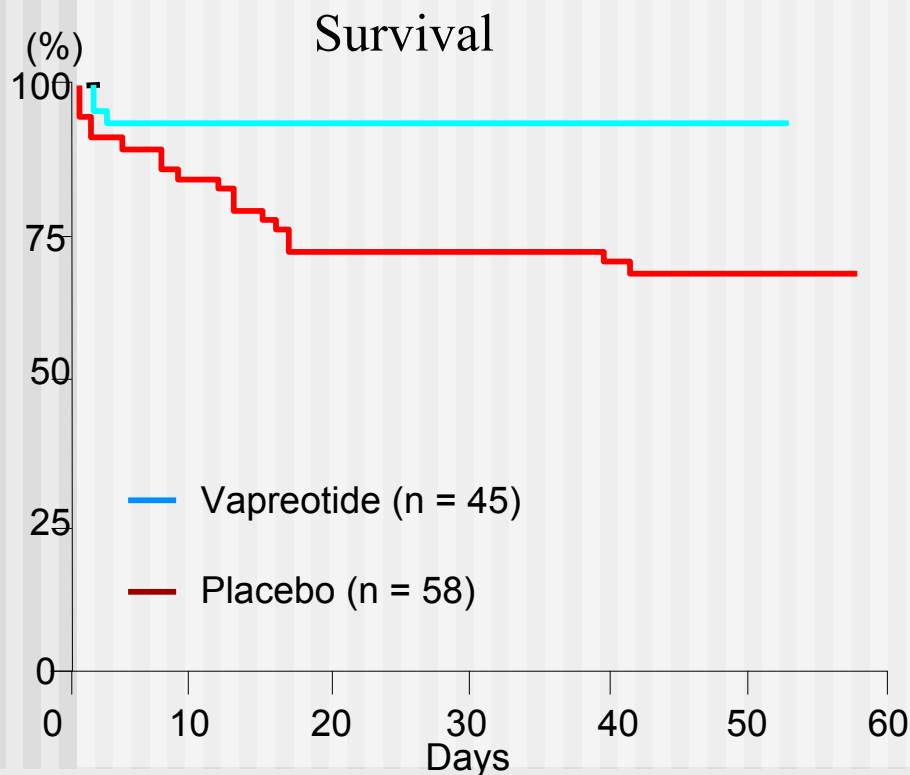
Treating of the acute bleeding episode

Pharmacological treatment Worldwide

	Europe, SE Asia Latin America	USA + Canada	Baveno V Vote n= 130
Terlipressin	96%	10%	61%
Somatostatin	61%	10%	23%
Octreotide	39%	70%	14%
Vapreotide	9%	20%	2

Variceal bleeding: Early administration of pharmacological treatment improve survival

Subgroup of patients with unstable hemodynamics at admission:
HR > 100 b/mn or SBP < 80 mmHg



Treating of the acute bleeding episode

Timing of Endoscopy

- Endoscopy should be considered as soon as possible after initial restitution (within 12 h of admission) especially in patients with clinically significant bleeding
- In mild bleeds causing neither haemodynamic changes nor requiring volume restitution, endoscopy can be done electively (24h)

Rupture de VO ou V. Gastriques

Traitement Endoscopique

- Sclérothérapie

- Injection para ou intravariqueuse (VO) d'une substance sclérosante (Aetoxysclérol, Oléate d'Ethanolamine, Tétradécyl Sulfate de Sodium ou Morrhuate de Sodium, Alcool absolu)
- l'Obturation des VO ou VG par injection intravariqueuse d'une colle : cyanoacrylate (Bucrylate ®, Histoacryl®).

- Ligature endoscopique VO

- Alternative à la sclérothérapie
- Efficacité comparable sur l'hémostase
- Tendance moindre aux complications sévères

RUPTURE DE VARICES OESOPHAGIENNES

Ligature élastique vs Sclérothérapie

9 études contrôlées et randomisées (288 patients)

Auteurs	Année	Ligature	Sclérose	Echecs %	Mortalité %
Stiegmann	1992	14	13	14-23	-
Laine	1993	9	9	11-11	-
Gimson	1993	21	23	10-9	-
Jensen	1993	14	11	20-0	-
Lo	1995	18	15	6-20	-
Hou	1995	20	16	0-12	-
Fakhry	1995	10	12	10-8	10-8
Sarin	1997	5	7	20-14	-
Lo	1997	37	34	3-24	19-38
Total		140	148	4-19	17-30
RR cumulé (CI: 95%)				0,56 (0,27-1,14)	N.A

Treating of the acute bleeding episode

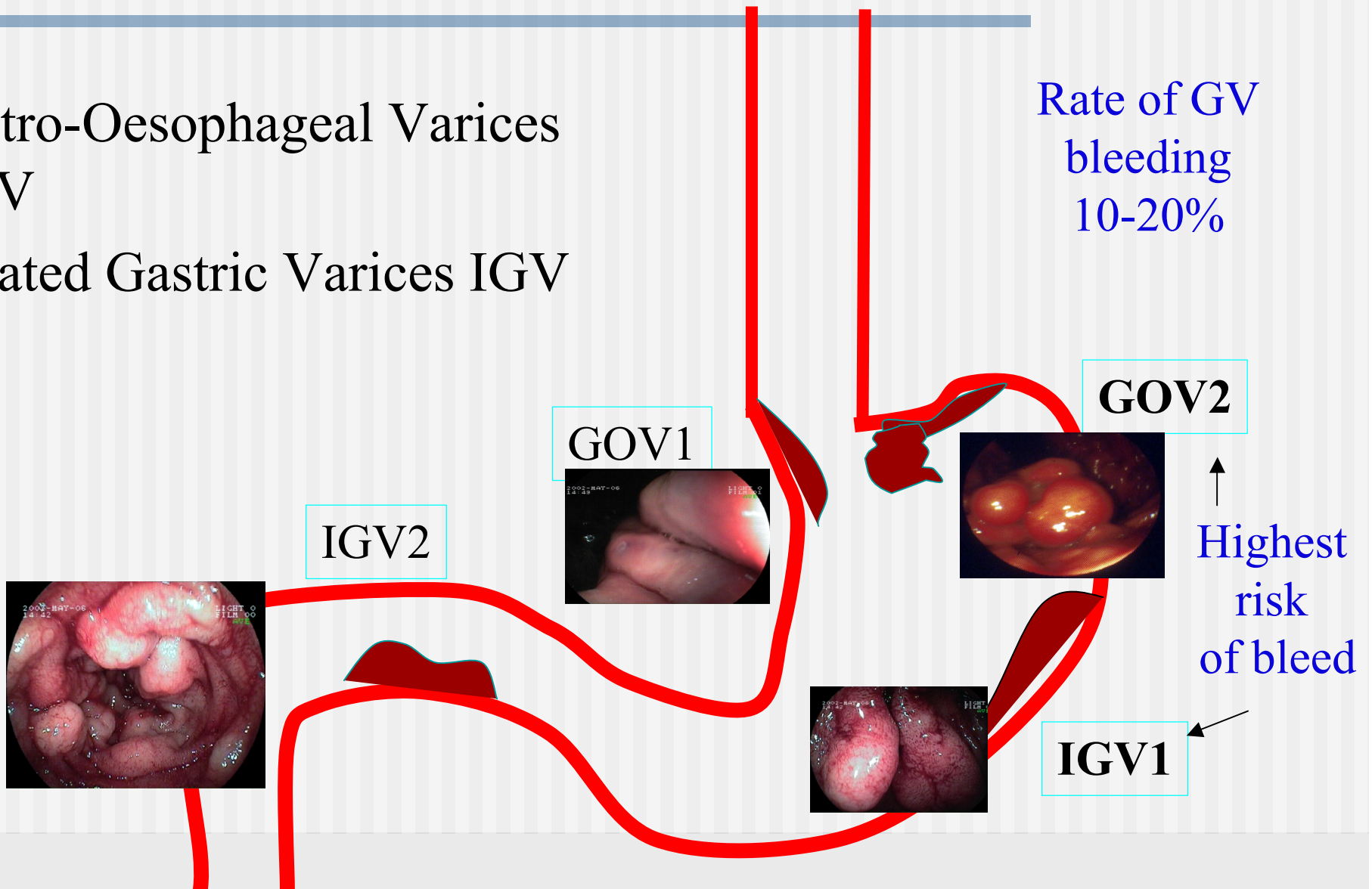
Endoscopy treatment :

- Ligation (EVL) is the recommended form of endoscopic therapy for acute esophageal variceal bleeding although the sclerotherapy may be used in actively bleeding patients if ligation is technically difficult.
- Endoscopic treatment with tissue adhesive (ie. N-butyl cyanoacrylate) is recommended for acute gastric variceal (IGV) (1b;A) and those gastroesophageal varices type 2 (GOV2) that extend beyond the cardia (5;D).

Classification of Gastric Varices

- Gastro-Oesophageal Varices GOV
- Isolated Gastric Varices IGV

Rate of GV bleeding
10-20%



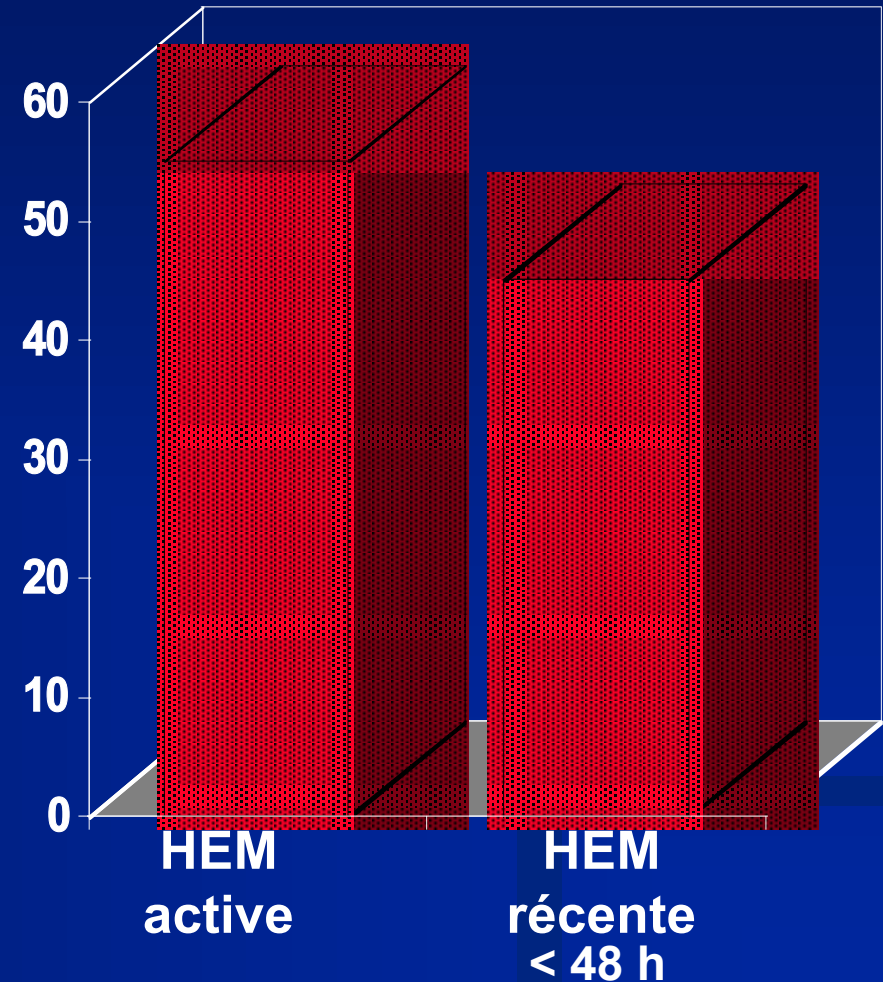
Obturation des Varices Oesophagiennes au Cyanoacrylate en traitement de l'hémorragie

Hémorragie active

138 patients (55 %)

Hémorragie récente
< 48 heures

113 patients (45 %)



OBTURATION DES VO EN URGENCE AU CYANOACRYLATE RESULTATS

Hémostase définitive

87%

- 1 séance : 72%
- 2 séances : 15%

Obturation	Récidive	Mortalité
Hémorragie active	24%	28%
Hémorragie récente (48 heures)	9%	4%

Obturation des Varices Gastriques en Urgence

42 Patients Cirrhotiques

Child A: 8 (19%), Child B: 6 (14%), Child C: 28 (67%)

Hémorragie active
29 pts (69%)

Hémorragie récente (48h)
13 pts (31%)

Hémostase définitive

37 patients 88%

Récidive hémorragique
(1 mois)

6 /37 patients (16%)

Mortalité
(1 mois)

9/42 patients (21%)

HEMORRAGIE PAR RUPTURE DE VARICES GASTRIQUES

Sclérose vs Cyanoacrylate vs Ligature ETUDE PROSPECTIVE RANDOMISÉE CHEZ LE CHIEN

	LIGATURE 20	SCLEROSE 20	OBTURATION 19	p
ULCÉRATION (1 semaine)	100%	60%	30%	< 0,05
HEMORRAGIE (par ulcère)	30%	5%	5%	< 0,05
HEMORRAGIE (abondante)	15%	0%	0%	< 0,05

R. JUTABHA et al (Gastrointest Endosc 1995; 41(3): 206-11)

Surgery / TIPS in acute bleeding

■ Surgery :

- Orloff et al, J Am Coll Surg 2009

■ Early TIPS

Early PTFE-TIPS versus Conventional Therapy in Patients at High risk of Failure

A multicenter European study

63 cirrhotic patients with Acute Variceal Bleeding
(Child-Pugh B+active bleeding or Child-Pugh C)

Vasoactive drugs+Endoscopic treatment+Antibiotics

Randomization

24h of Admission

Standard therapy for 5 days

Then Secondary prophylaxis

EBL+BL

n= 31 patients

If failure PTFE-TIPS
as Rescue treatment

Early PTFE-TIPS

(10mm)

n= 32 patients

within 24 hrs : 19 pts

48 hrs : 10 pts

72 hrs : 3 pts

Early PTFE-TIPS versus Conventional Therapy in Patients at High risk of Failure

A multicenter European study

	Early PTFE-TIPS n= 32	Standard Therapy n=31	p
Free From failure to control active variceal bleeding or preventing rebleeding (12 months)	97%	50%	
Survival at 6 weeks	96%	67%	<0.001
Survival at 12 months	86%	60%	<0.001

Early TIPS in acute bleeding

- An early TIPS within 72 hours (ideally < 24 hours) should be considered in patients at high- risk of treatment failure (e.g. Child-Pug class C < 14 points or Child class B with active bleeding) after initial pharmacological and endoscopic therapy. (1b;A)
- **Baveno V vote:**
 - Who put Early TIPS for acute bleeding without endoscopy
 - Child C : 6%
 - Child B active bleeding 7%
 - Both : 29%
 - Never: 57%

Oesophageal Stent

- Uncontrolled data suggest that self-expanding covered esophageal metal stents may be an option in refractory esophageal variceal bleeding, although further evaluation is needed .

(4;C)

Treating of the acute bleeding episode

Refractory bleeding

- Persistent bleeding despite combined pharmacological and endoscopic therapy is best managed by TIPS with PTFE-covered stents. (2b;B)
- Rebleeding during the first 5 days may be managed by a second attempt at endoscopic therapy. If rebleeding is severe, PTFE-covered TIPS is likely the best option. (2b;B)

Traitement Préventif de la Récidive hémorragique

Prophylaxie Secondaire

Traitement Préventif de la Récidive hémorragique

Prévention Secondaire

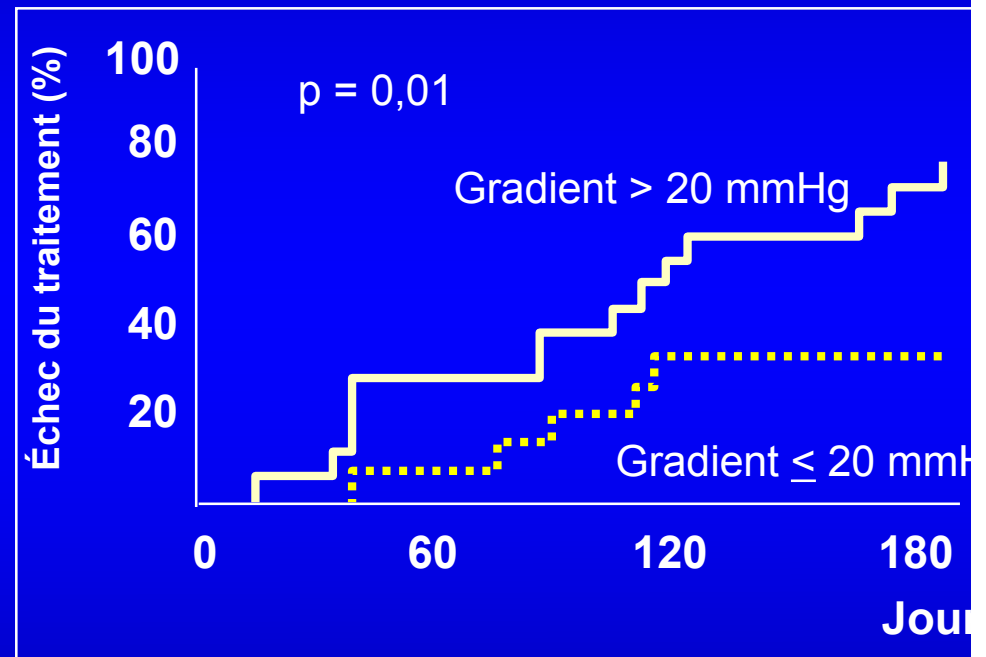
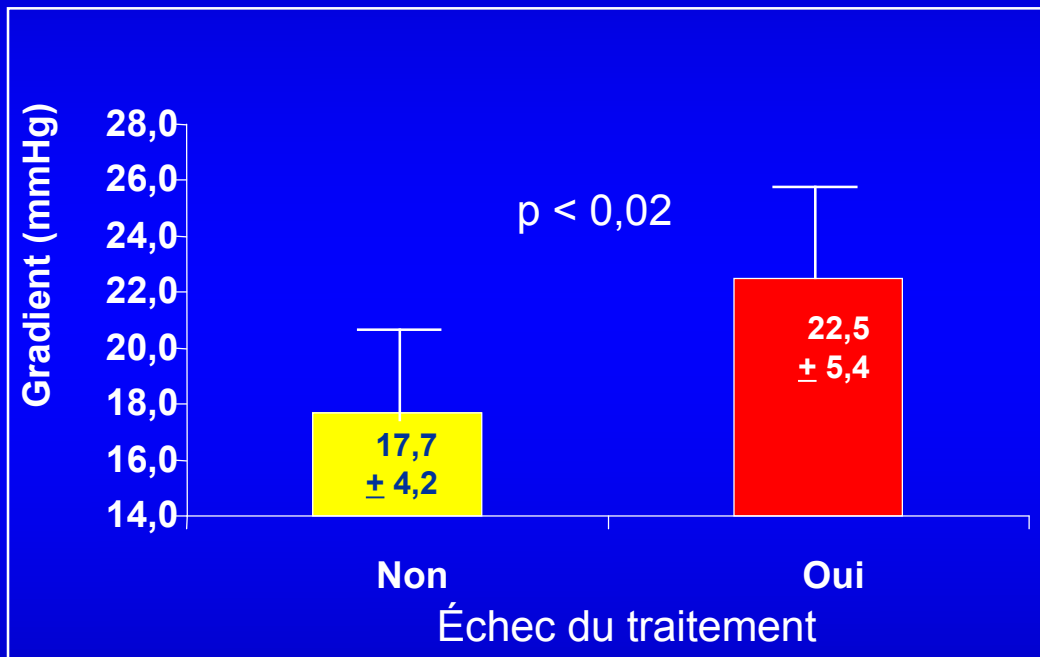
Récidive hémorragique sans traitement

42% à 6 semaines

70% dans l'année

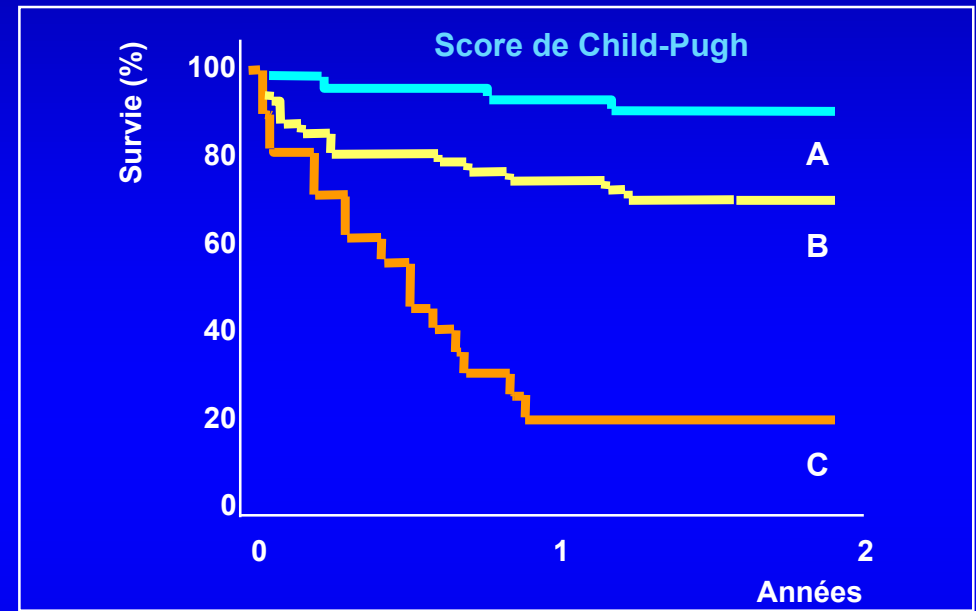
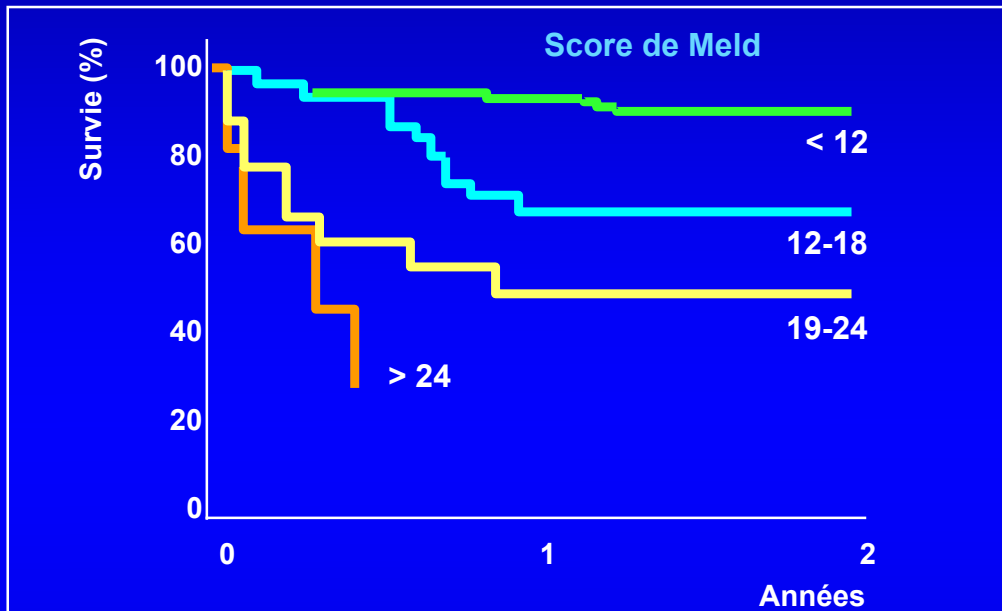
La mesure du gradient pourrait prédire la récurrence des varices œsophagiennes (VO)

- Étude hémodynamique chez 33 malades après ligature de VO



- L'échec thérapeutique (récidive hémorragique < 6 mois, ou récurrence endoscopique des varices < 6 mois, ou absence d'éradication au bout de 5 séances), était observé dans 64 % des cas dont 66 % par récurrence endoscopique précoce
- Un gradient > 20 mm Hg était associé à l'échec du traitement

Le Meld ou le gradient font-ils mieux que le Child pour prédire la survie du patient cirrhotique après hémorragie digestive ?



Cette étude rétrospective a évalué les valeurs pronostiques des scores de Meld, de Child et de la mesure du gradient de pression hépatique dans les 7 jours suivant une hémorragie digestive chez 144 malades cirrhotiques

En analyse univariée, le Meld ($p < 0,001$), la mesure des pressions ($p = 0,05$) et le score de Child ($p < 0,001$) étaient des valeurs pronostiques de la survie

- Ces variables n'ont pas été testées en analyse multivariée

Time to start secondary prophylaxis

- Secondary prophylaxis should start as soon as possible from day 6 of the index variceal episode
(5, D)
- The start time of secondary prophylaxis should be documented

Prevention of Rebleeding

β-blockers vs no treatment

2 meta-analysis, 13 RCT:

- Rebleeding at 2 yrs : 68% to 48% (p <0.01)
- Survival at 2 yrs : increased 67% to 74% (p <0.05)

Prevention of Rebleeding

β -blockers vs β -blockers + ISMN

- In favor of β -blockers alone

	β -blockers / β -blockers + ISMN	• β -blockers / β -blockers + ISMN
	Rebleeding (%)	■Mortality (%)
Gournay N = 95	55/40 NS	22/24 NS
Patti N = 104	39/51 NS	14/32 p = 0.02
Zang N = 66	40/20 NS	NS

Prevention of Rebleeding

Sclerotherapy vs no treatment

Meta-analysis (8 RCT, 1111 patients)

- In favor of sclerotherapy
 - Rebleeding : RR 0.63 (0.5-0.8)
 - Death : RR 0.77 (0.6-0.98)

Prevention of Rebleeding

■ Sclerotherapy vs β -blockers

2 meta-analysis, 11 RCT, 971 patients

■ No significant difference between treatments

- Rebleeding : RR 0.88 (0.58-1.32)

- Mortality : RR 0.95 (0.58-1.32)

- Adverse events : RR 0.85 (0.65-1.11)

Prevention of Rebleeding

■ Sclerotherapy + β -blockers vs Sclerotherapy

Meta-analysis, 12 RCT, 853 patients

■ In favor of combined treatment

- Rebleeding : RR 0.54 (0.34-0.86)

- Mortality : RR 0.65 (0.43-0.97)

Prevention of Rebleeding

Band Ligation vs β -blockers

- No difference between treatments

	Ligation / β -blockers + ISMN	Ligation / β -blockers + ISMN
	Rebleeding (%)	Mortality (%)
Villanueva (2001) N = 144	49/33 p <0.05	42/32 NS
Lo (2002) n= 121	38/57 NS	25/13 NS
Patch (2002) n= 102	53/37 NS	22/33 NS

Prevention of Rebleeding

Band Ligation vs Sclerotherapy

	Sclerotherapy	Band Ligation
Rebleeding 20 RCT	35%	24%
Mortality 19 RCT	23%	20%
Obliteration 17 RCT	80%	77%
Recurrence of varices 10 RCT	19%	27%

Prevention of Rebleeding

Band Ligation vs Sclerotherapy

Meta-analysis (18 RCT, 1509 patients)

In favor of Band Ligation :

- Rebleeding : RR 0.54 (0.43 - 0.68)
- Complications : RR 0.3 (0.19 - 0.46)
- Death : RR 0.78 (0.59 - 1.02)
- Obliteration : RR 1.23 (0.93-1.92)
- Fewer sessions in BL 2.7 - 4.1 vs 4 - 6.5 in ST
- Variceal recurrence rate higher after BL:
 - RR 1.48 (1.03 -2.12)

Prevention of Rebleeding

Band Ligation vs Band Ligation + sclerotherapy

Meta-analysis : 7 RCT, 453 patients

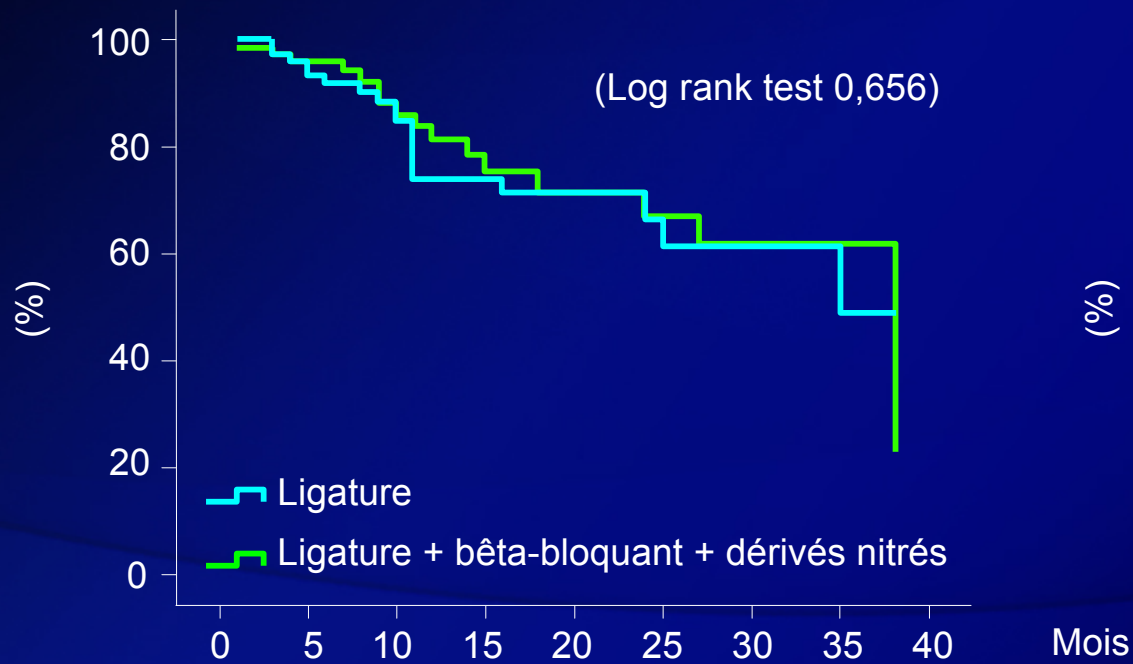
No difference between treatments

- Rebleeding : RR 1.12 (0.69 - 1.81)
- Mortality : RR 1.1 (0.7 - 1.74)
- But higher incidence of esophageal stricture in combination therapy ($p < 0.001$)

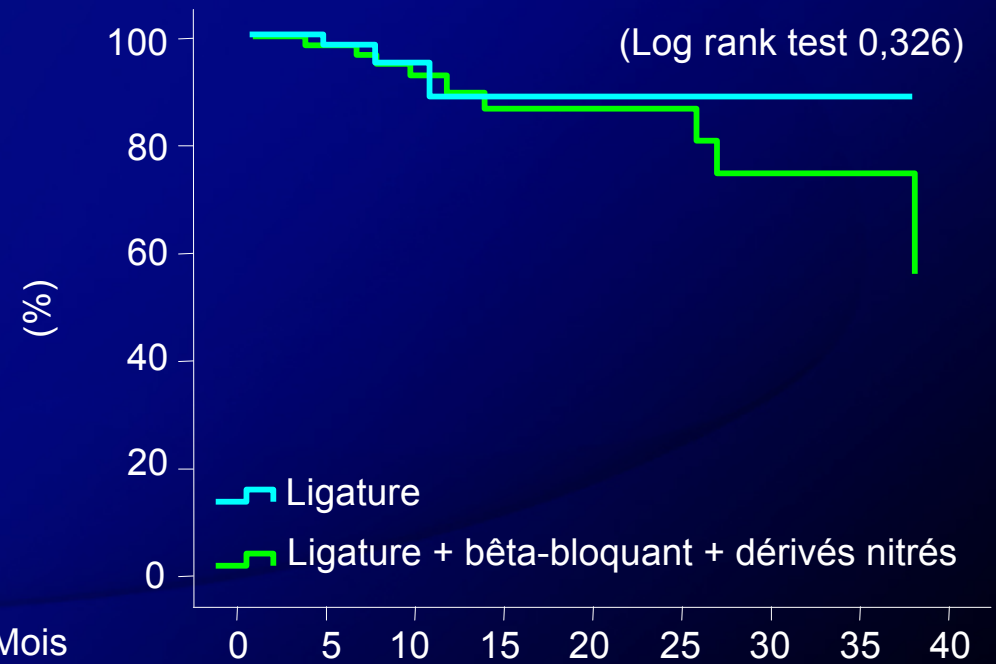
Prévention de la récurrence hémorragique : Ligature versus Ligature + bêta-bloquants + nitrés

Prévention de la récurrence hémorragique chez les malades atteints de cirrhose
Étude randomisée : ligature (n = 88) versus ligature + propranolol + dérivé nitré (n = 80)

Risque de récurrence hémorragique



Survie



Prevention of Rebleeding

TIPS vs β -blockers +ISMN

1 Study: Escorsell (2002) 91 patients

No difference between treatments

- Rebleeding at 2 years : 13% vs 39% ($p < 0.05$)
- Mortality : 28% vs 25% NS
- But less encephalopathy, more frequent improvement in Child' Pugh score and lower cost in drug therapy

Prevention of Rebleeding

TIPS vs Endoscopic therapy

Meta-analysis, 13 RCT, 948 patients (Median follow-up 10-32 m.)
(Sclerotherapy 8, band ligation 5, in addition to propranolol 4 studies)

- Rebleeding significantly reduced by TIPS : OR 3.3 (2.3-4.7)
- No difference in Mortality : OR 0.87 (0.65-1.17)
- Less encephalopathy after endoscopic treatment : OR 0.48 (CI 0.34-0.67)

Prevention of Rebleeding

TIPS vs H-graft Portacaval shunt (8mm)

Rosemurgy AS et al (2000) (Median follow-up 4 years)

	TIPS N = 66	HG PCS N = 66	p
Rebleeding	16%	3%	0.01
Liver transplantations	7.5%	0	0.01
Late death	33.9 %	13.2%	NS
Treatment Failure	64%	35%	0.01

Higher cost in TIPS

Prevention of Rebleeding

TIPS (uncovered stent) vs Distal spleno renal Shunt)

Henderson et al (not yet published) (Median follow-up 42 months)

	DSRS N = 73	TIPS N = 63	Total N = 140
Child A/B	41/32	39/28	80/60
Rebleeding	6%	9%	
Reintervention	11%	82%	P < 0.001

Similar in both groups :

Encephalopathy : 20% at 1 yr, 50% at 5 yrs (at least 1 episode)

Survival : 90% at 1 yr and 65% at 5 yrs

Prevention of Rebleeding

1. In patients with cirrhosis who have not received primary prophylaxis :

- Combination of beta-blockers and band ligation is the preferred therapy as it results in lower rebleeding compared to either therapy alone (1a;A)
- Hemodynamic response to drug therapy provides information about rebleeding risk and survival (1a;A)
- The addition of ISMN to beta-blockers may improve the efficacy of treatment in hemodynamic non-responders(5;D)
- IF no EVL : Beta-blockers with Isosorbide Mononitrate is the preferred option (1a;A)

Prevention of Rebleeding

2. In patients with cirrhosis who are on β -blockers for primary prevention and bled,

- Endoscopic band ligation is the preferred treatment
- In patients who have Contraindications or Intolerance to β -blockers, band ligation is the preferred for treatment for prevention of rebleeding

Prevention of Rebleeding

3. For patients who fail endoscopic and pharmacological treatment for prevention of rebleeding :

- TIPS with PTFE-covered stents is effective and is the preferred option. Surgical shunt in Child-Pugh A and B patients is an alternative if TIPS is unavailable. (2b;B)
- Transplantation provides good long-term outcomes in appropriate candidates and should be considered (2b;B)
- TIPS may be used as a bridge to transplantation (4;C)

Prevention of Rebleeding

4. In patients who have bled from IGV 1 or GOV 2 gastro-esophageal varices :

- N-butyl-cyanoacrylate (1b;A) or TIPS (2b;B) are recommended
(B-Blockers removed)
- Patients who have bled from gastro-esophageal varices (GOV1) may be treated with glue, band ligation or β -blockers (2b;B)

Prevention of Rebleeding

5. In patients who have bled from portal hypertensive gastropathy

- β -blockers (A,1b) should be used for prevention of recurrent rebleeding
- In patients in whom β -blockers are contraindicated or failed and who cannot be managed by conservative therapy
 - TIPS (C,4) or Selective shunts (C,4) should be considered

The END

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therapy of
the esophageal
varices

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