

Portal Hypertension and its complications

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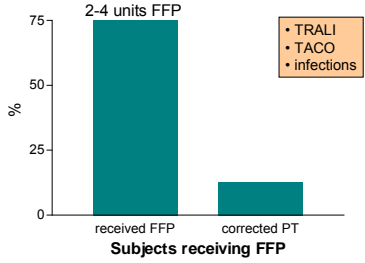
Case 1

- A 42 yr male with long standing h/o HCV and heavy alcohol use is admitted with a history of vomiting blood and passing out. At admission, he is combative and vital signs show pulse= 110/min, BP= 80/50. The initial labs are:
 - Hgb: 7 gm/dl
 - INR: 1.4
 - Platelets: 70K
 - WBC: 9600 with left shift
 - AST: 250 IU/l
 - ALT: 210 IU/L
 - Bilirubin: 3.6 mg/dl
 - Creatinine: 1.4 mg/dl

Question # 1

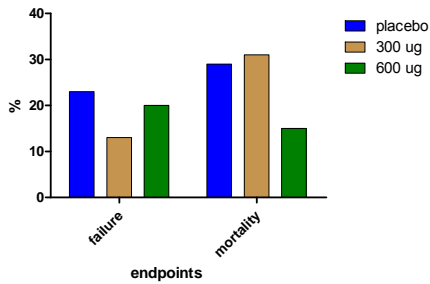
- What initial resuscitative measures are appropriate:
 - packed red cells (3 units)
 - FFP (3 units)
 - platelet transfusion
 - recombinant factor VII

Efficacy of FFP in correcting coagulopathy



Youssef et al, Am J Gastroenterol, 2003, 98:1391-1394

Recombinant factor VII for active variceal hemorrhage

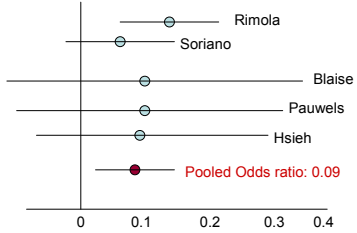


Bosch et al, Hepatology, 2008; 47:1604-14

What other measures are important

- Antibiotics:
 - routinely
 - if cultures are positive
 - if WBC is > 11k or fever present
 - if chest x-ray shows fluffy shadows suggestive of aspiration

Antibiotics improve survival in acute variceal hemorrhage

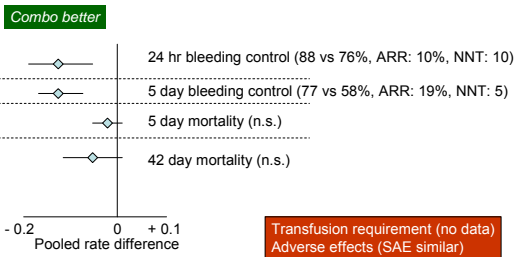


Bernard B. Hepatology 1999; 29:1655-61.

What is the best definitive treatment

- Endoscopic band ligation
- Endoscopic sclerotherapy
- Octreotide or terlipressin
- Octreotide + band ligation

Meta-analysis of combination therapy vs endoscopic Rx for acute variceal hemorrhage



Adapted from Banares et al, Hepatology, 2002, 35:609-615, and Laine et al, Baveno IV proceedings

Decision points

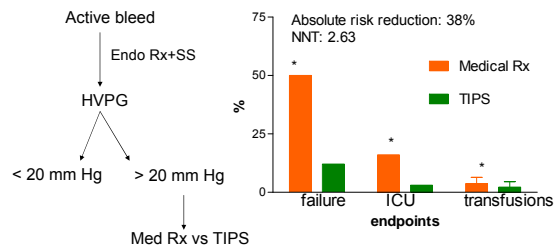
- 12 hours after EVL and after octreotide is started, HR is 100/min, BP is still 88/50. N/G tube shows bright red blood. What to do:
 - repeat EVL
 - protect airway
 - Balloon tamponade
 - TIPS

Transjugular intrahepatic portosystemic shunts (TIPS)

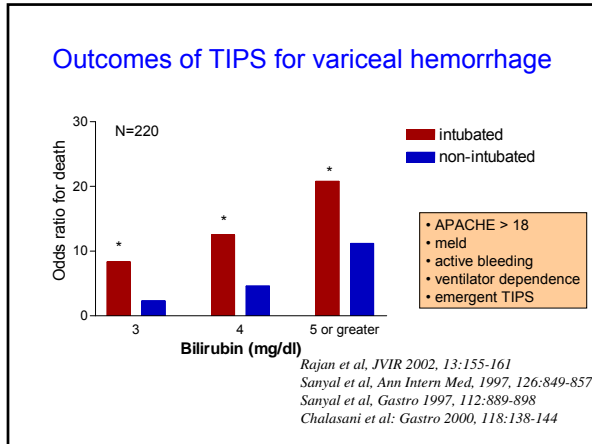


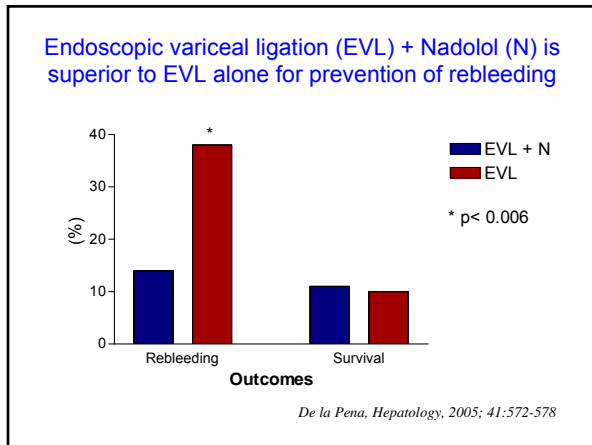
- Controls active hemorrhage (> 90%)
- effective for both esophageal and gastric varices

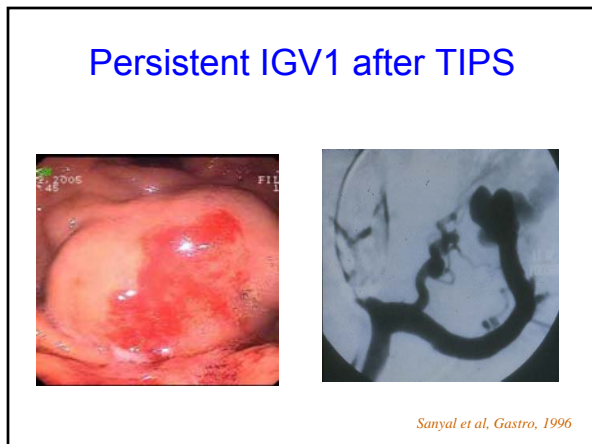
Role of early TIPS

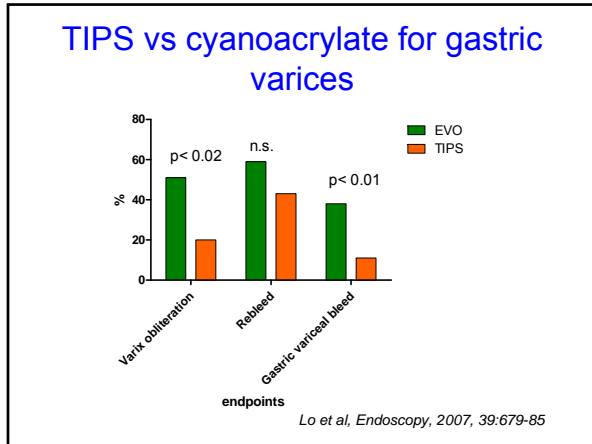


Monescillo et al, Hepatol, 2004, 40:793-801









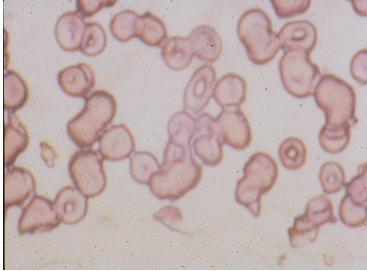
Case continued

- Patient survives the bleed after TIPS and is discharged home after day 6. He is readmitted 10 days later with confusion, disorientation and asterixis. On examination, he is pale and jaundiced. Family denies any overt bleeding.
- Labs show:
 - Hgb: 7 gm/dl
 - Bilirubin: 6 gm/dl
 - INR: 1.4
 - creatinine: 1.5

Why is the hemoglobin low?

- GI bleeding (? Hemobilia)
- Hemolysis:
 - TIPS-induced
 - Spur cell anemia
 - Zieve's syndrome

TIPS induced hemolysis



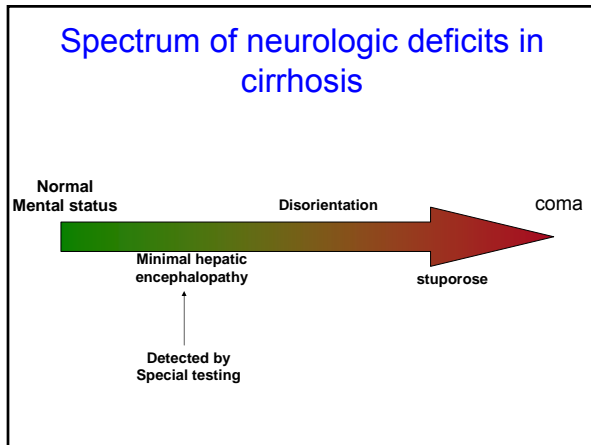
What to do?

- Close the shunt
- Transfuse to bring Hgb to 9 gm/dl
- No intervention required
- Anti-oxidant therapy with high dose vitamin E

TIPS associated hemolytic anemia

- Affects about 10% of subjects
- **Clinical presentation:**
 - drop in Hgb by 2-3 gm
 - increase in indirect bilirubin
 - occasionally causes severe anemia and high-output failure
- **Treatment:**
 - usually none required
 - rarely liver transplant

Nomenclature of Hepatic Encephalopathy			
HE Type	Nomenclature	Subcategory	Subdivisions
C	HE associated with cirrhosis and PHTN / or portalsystemic shunts	Episodic HE	Precipitated Spontaneous Recurrent
		Persistent HE	Mild Severe Treatment-dep.
		Minimal HE	



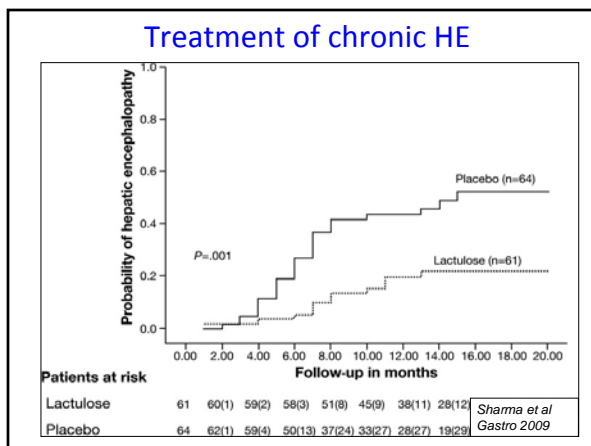
MHE predicts development of OHE

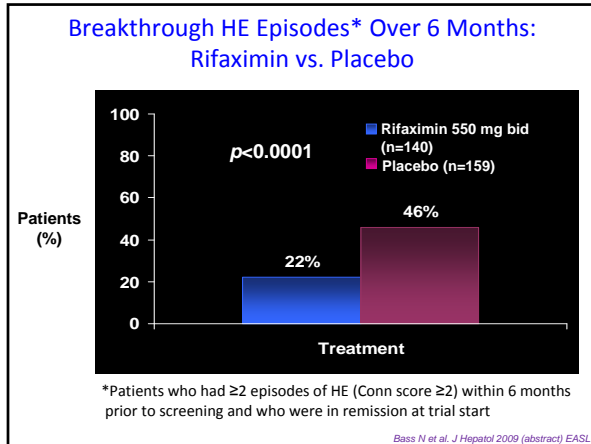
Author	n	Duration	Rate of OHE (MHE + vs MHE-)	P value
Hartmann	116	29 mths	56 vs 8	<0.01
Bajaj	125	36 mths	25 vs 0	<0.001

Author	Duration	Improved MHE markers	Testing of clinically relevant outcomes
Watanabe	8 weeks	Yes	–
Li	24 weeks	Yes	–
Horsmans	2 weeks	Yes	–
Prasad	90 days	Yes	Improved quality of life
Morgan	8 weeks	Yes	–
Bajaj	60 days	Yes	Trend: reduced OHE
Liu	60 days	Yes	CTP improvement
Malguanera	90 days	Yes	–

Overt HE: Precipitating Factors

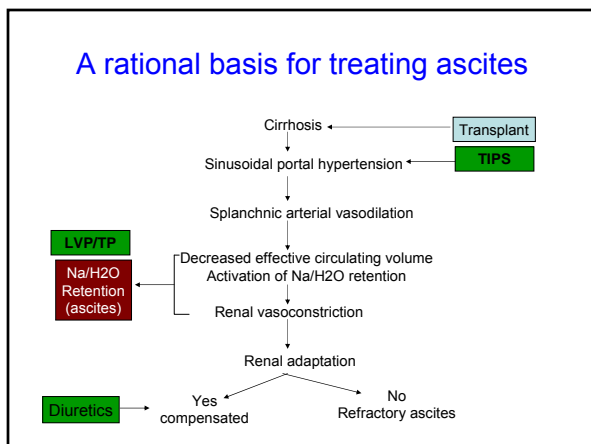
- Gastrointestinal bleeding
- Infection
- Sedative drugs
- Hyponatremia
- Non-adherence
 - Fluid restriction
 - Diuretics
 - Vomiting or diarrhea
- Dehydration





Case continued

- The patient was given lactulose, PPI, put on protein restriction and the TIPS was reduced. Rpt endoscopy was unremarkable. He became more oriented and vital signs stabilized. He is then discharged. Two weeks later he is seen in clinic. At this time, he had developed ascites and edema.
- Hgb: 8 gm/dl
- WBC: 8000/mm³
- Bilirubin: 7 gm/dl
- Albumin: 2.5 gm/dl
- Creatinine: 1.7 mg/dl
- Na: 126 meq/l



Initial approach to ascites

- Na restriction + diuretics:
 - Na (88 meq/day)
 - use combination of loop-acting and distal acting diuretics when feasible
- Slow
- Does not affect survival
- Large volume paracentesis (LVP):
 - > 5 liters
- Fast
- High rate of recurrence
- Does not affect survival
- Requires albumin infusion to prevent post paracentesis circulatory dysfunction

Case continued

- Patient started on Na restriction and spironolactone (100 mg/day) and a LVP is performed. Patient is discharged but returns after 5 days with tense ascites.
 - Bilirubin: 6 mg/dl
 - Albumin: 2.2 gm/dl
 - INR: 1.6
 - Creatinine: 2.4 mg/dl

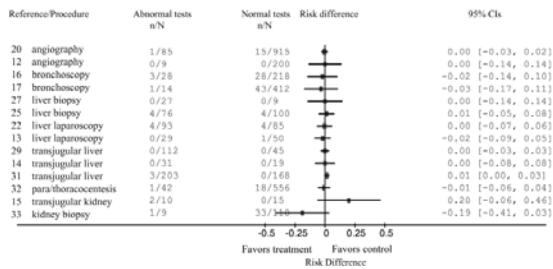
Next best steps

- Increase spironolactone (200 mg/day)
- Add furosemide (40 mg/day)
- Place another TIPS
- LVP + i.v. albumin

Traditional coagulation parameters do not predict bleeding risk in cirrhotics

- INR, platelets, TEG do not predict ulcer or procedure related bleeding after EVL. (*Da Rocha et al, CGH, 2009*)
- INR, platelets do not predict peri- or post-paracentesis hemorrhage (*Grabau et al, Hepatology, 2004, Lin et al, Dig Liv Dis 2005*)

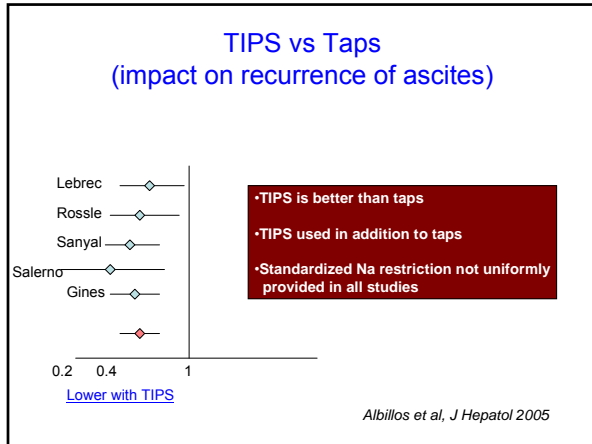
INR has no correlation with bleeding risk after procedures

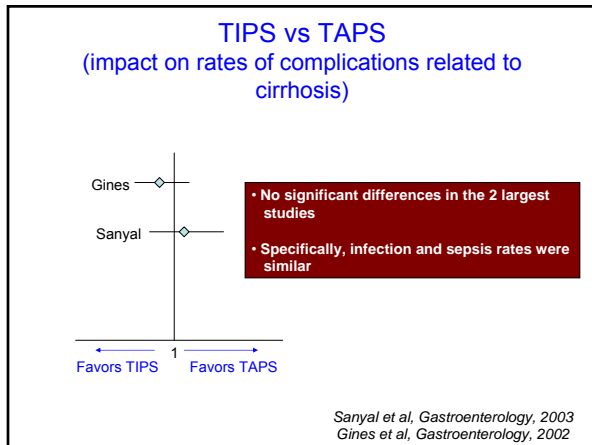


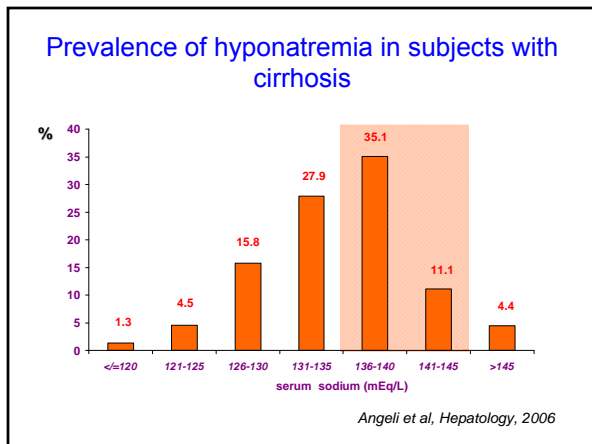
Segal and Dzik, *Transfusion*, 2005, 45:1413-1425

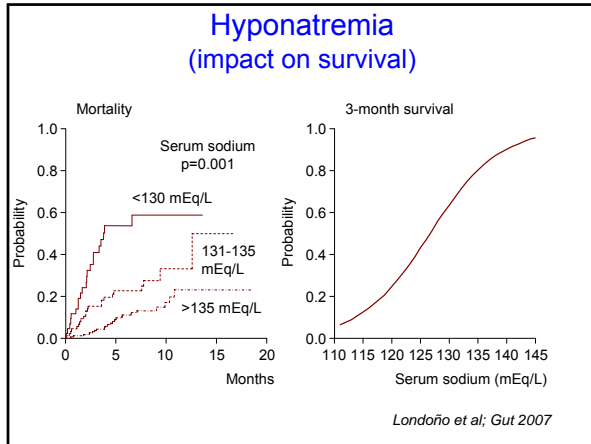
Refractory Ascites
International Ascites Club Criteria

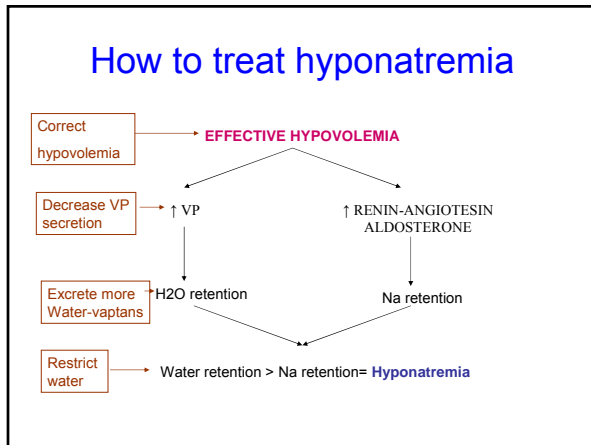
- **Diuretic Resistant:** failure to lose at least 1.5 Kg/wk on:
 - 400 mg Spironolactone
 - 160 mg furosemide
- **Diuretic intractable:** failure to lose weight due to inability to use effective doses because of diuretic side effects.











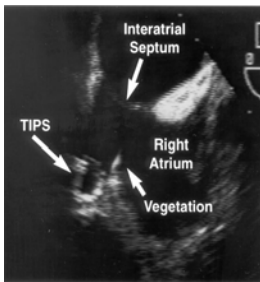
Case-continued

- Patient undergoes another LVP + i.v. albumin. Diuretics are held for a day and then restarted at a lower dose. Patient is counseled about Na restriction. He is discharged but returns in 7 days with tense ascites and fever, altered ms, and shortness of breath.
 Pulse= 90/min
 BP: 90/50
 Bilirubin: 9 mg/dl
 Creatinine: 3.5 mg/dl
 3 out of 3 blood cultures are positive for enterococci

Type and Frequency of Injury in Acute Renal Failure in Cirrhosis

Type	Frequency
ATN (ischemic)	Common
Prerenal failure	
Decreased volume	Very common
HRS	Relatively common
Drugs	Relatively common
Obstruction	Uncommon
Intrinsic	Uncommon

Infective Endocarditis



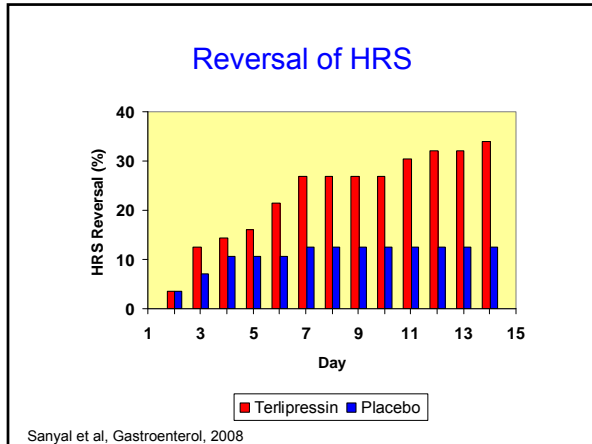
- **Diagnostic features:**
 - Continuous bacteremia
 - TIPS vegetation or thrombus
 - No other source of bacteremia
 - Septic pulmonary emboli
- **Treatment:**
 - gram negative bacterial coverage
 - Skin contaminants
 - Anaerobic coverage in gas in portal system

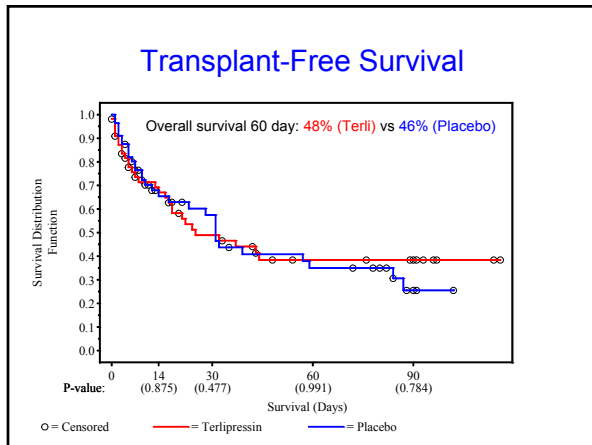
Sanyal et al, Gastroenterol, 1998; 115:110-115

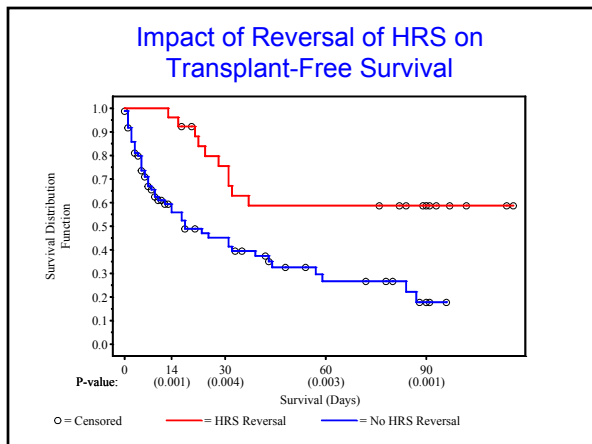
Hepatorenal syndrome

Salerno et al, Gut, 2007, epub March 2007

- Cirrhosis with ascites
- Serum creatinine > 1.5 mg/dl
- No improvement after at least 2 days of diuretic withdrawal and volume replacement with albumin
- No nephrotoxic drugs used
- Absence of intrinsic renal disease







Factors associated with failure to respond to terlipressin

- Baseline creatinine > 6 mg/dl
- Duration of therapy < 48 hrs
- Ventilator support due to multi-organ dysfunction

Utility of vasoconstrictors for HRS

	Midodrine	Terlipressin	Norepinephrine
Rationale:	++	+++	++
Route:	Oral + octreotide	i.v. slow bolus	i.v. infusion
Clinical effectiveness:	Uncontrolled	Phase III RCT + phase II RCT	Phase II RCTs
Level of monitoring:	no special needs	Monitored bed	ICU bed
Safety:	GI, piloerection	GI, ischemia	Ischemia, GI, ARDS
Cost:	↑	?	↑↑↑

Circulatory failure drives progression from ascites to HRS

