The acutely bleeding cirrhotic

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The Newcastle upon Tyne Hospitals NHS
NHS Foundation Trust

Introduction

- GI bleeding is a common presenting feature for patients with cirrhosis
- Current UK 30 day mortality is 15% for patients with acute variceal bleeding.
- Mortality falling – 40% in 1980s
- Major risk factors for mortality
  - Child-Pugh C cirrhosis (40% mortality)
  - Active bleeding on admission
  - Associated infections
  - Portal vein thrombosis
  - Higher portal pressure

Causes of bleeding in a cirrhotic patient

- Portal hypertension related
  - Oesophageal or Gastric varices (60-65% of bleeds)
  - Portal hypertensive gastropathy
  - GAVE
- Non-portal hypertension related
  - Peptic ulceration
  - Mallory Weiss Tear
  - Erosive oesophagitis/gastritis/duodenitis
  - Cancers
  - others

Case

- 49 year old male
- Presented with haematemesis
- Known alcohol related liver disease
- Sporadic attendance at follow up
- Last clinic letter stated “clinically cirrhotic”
- Drinking 100 units per week (had ‘cut down’ recently)
- Medications:
  - Thiamine 100mg od
  - Propranolol 40mg BD (for ‘anxiety’)
- Examination:
  - Pulse 72/min, BP 84/43, significant postural drop in BP
  - GCS 15/15
  - Moderate ascites
  - Melaena on PR

Case (2)

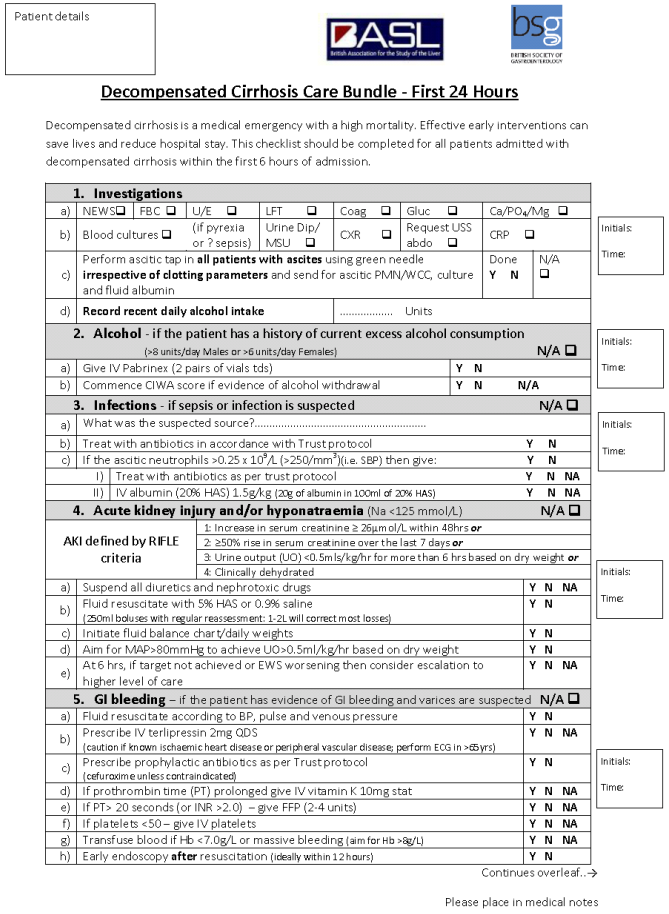
- Bloods
  - Hb 66
  - WCC 5.2
  - Platelets 75
  - PT 24 secs

  - Bilirubin 124
  - Albumin 28
  - ALT 25

  - Na 131
  - K 3.6
  - Urea 10.2
  - Creatinine 140

  - CRP 6

Cirrhosis care bundle



Patient details

Decompensated Cirrhosis Care Bundle - First 24 Hours

Decompensated cirrhosis is a medical emergency with a high mortality. Effective early interventions can save lives and reduce hospital stay. This checklist should be completed for all patients admitted with decompensated cirrhosis within the first 6 hours of admission.

1. Investigations									
a)	NEWS❑	FBC ❑	U/E ❑	LFT ❑	Coag ❑	Gluc ❑	Ca/PO4/Mg ❑		
b)	Blood cultures ❑ (if pyrexia or ? sepsis)		Urine Dip/ MSU ❑	CXR ❑	Request USS abdo ❑	CRP ❑			
c)	Perform ascitic tap in **all patients with ascites** using green needle **irrespective of clotting parameters** and send for ascitic PMN/WCC, culture and fluid albumin					Done **Y N**	N/A ❑		
d)	**Record recent daily alcohol intake** ..... Units								
2. Alcohol - if the patient has a history of current excess alcohol consumption (>8 units/day Males or >6 units/day Females)							N/A ❑		
a)	Give IV Pabrinex (2 pairs of vials tds)					**Y N**			
b)	Commence CIWA score if evidence of alcohol withdrawal					**Y N**	**N/A**		
3. Infections - if sepsis or infection is suspected							N/A ❑		
a)	What was the suspected source?.....								
b)	Treat with antibiotics in accordance with Trust protocol						**Y N**		
c)	If the ascitic neutrophils >0.25 x 10^9/L (>250/mm^3)(i.e. SBP) then give:						**Y N**		
I)	Treat with antibiotics as per trust protocol						**Y N NA**		
II)	IV albumin (20% HAS) 1.5g/kg (20g of albumin in 100ml of 20% HAS)						**Y N NA**		
4. Acute kidney injury and/or hyponatraemia (Na <125 mmol/L)							N/A ❑		
AKI defined by RIFLE criteria	1: Increase in serum creatinine ≥ 26µmol/L within 48hrs ***or***								
	2: ≥50% rise in serum creatinine over the last 7 days ***or***								
	3: Urine output (UO) <0.5mls/kg/hr for more than 6 hrs based on dry weight ***or***								
	4: Clinically dehydrated								
a)	Suspend all diuretics and nephrotoxic drugs						**Y N NA**		
b)	Fluid resuscitate with 5% HAS or 0.9% saline (250ml boluses with regular reassessment: 1-2L will correct most losses)						**Y N**		
c)	Initiate fluid balance chart/daily weights						**Y N**		
d)	Aim for MAP>80mmHg to achieve UO>0.5ml/kg/hr based on dry weight						**Y N**		
e)	At 6 hrs, if target not achieved or EWS worsening then consider escalation to higher level of care						**Y N NA**		
5. GI bleeding – if the patient has evidence of GI bleeding and varices are suspected							N/A ❑		
a)	Fluid resuscitate according to BP, pulse and venous pressure						**Y N**		
b)	Prescribe IV terlipressin 2mg QDS (caution if known ischaemic heart disease or peripheral vascular disease; perform ECG in >65yr's)						**Y N NA**		
c)	Prescribe prophylactic antibiotics as per Trust protocol (cefuroxime unless contraindicated)						**Y N**		
d)	If prothrombin time (PT) prolonged give IV vitamin K 10mg stat						**Y N NA**		
e)	If PT> 20 seconds (or INR >2.0) – give FFP (2-4 units)						**Y N NA**		
f)	If platelets <50 – give IV platelets						**Y N NA**		
g)	Transfuse blood if Hb <7.0g/L or massive bleeding (aim for Hb >8g/L)						**Y N NA**		
h)	Early endoscopy **after** resuscitation (ideally within 12 hours)						**Y N**		

Initials: Time:

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Continues overleaf...→

Please place in medical notes

6. Encephalopathy			N/A ❑
a)	Look for precipitant (GI bleed, constipation, dehydration, sepsis etc.)	**Y N**	
b)	Encephalopathy – lactulose 20-30ml QDS or phosphate enema (aiming for 2 soft stools/day)	**Y N**	
c)	If in clinical doubt in a confused patient request CT head to exclude subdural haematoma	**Y N**	**N/A**
7. Other			
a)	Venous thromboembolism prophylaxis – prescribe prophylactic LMWH (patients with liver disease are at a high risk of thromboembolism even with a prolonged prothrombin time; withhold if patient is actively bleeding or platelets <50)	**Y N NA**	
b)	GI/Liver review at earliest opportunity (ideally within 24 hrs)	❑	

Initials: Time:

Initials: Time:

Name.....Grade.....Date.....Time.....

Decompensated Cirrhosis Care Bundle - First 24 Hours

The recent NCEPOD report 2013 on alcohol related liver disease highlighted that the management of some patients admitted with decompensated cirrhosis in the UK was suboptimal. Admission with decompensated cirrhosis is a common medical presentation and carries a high mortality (10-20% in hospital mortality). Early intervention with evidence-based treatments for patients with the complications of cirrhosis can save lives. This checklist aims to provide a guide to help ensure that the necessary early investigations are completed in a timely manner and appropriate treatments are given at the earliest opportunity.

- Decompensated cirrhosis is defined as a patient with cirrhosis who presents with an acute deterioration in liver function that can manifest with the following symptoms:
  - Jaundice
  - Increasing ascites
  - Hepatic encephalopathy
  - Renal impairment
  - GI bleeding
  - Signs of sepsis/hypovolaemia
- Frequently there is a precipitant that leads to the decompensation of cirrhosis. Common causes are:
  - GI bleeding (variceal and non-variceal)
  - Infection/sepsis (spontaneous bacterial peritonitis, urine, chest, cholangitis etc)
  - Alcoholic hepatitis
  - Acute portal vein thrombosis
  - Development of hepatocellular carcinoma
  - Drugs (Alcohol, opiates, NSAIDs etc)
  - Ischaemic liver injury (sepsis or hypotension)
  - Dehydration
  - Constipation

When assessing patients who present with decompensated cirrhosis please look for the precipitating causes and treat accordingly. The checklist shown overleaf gives a guide on the necessary investigations and early management of these patients admitted with decompensated cirrhosis and should be completed on all patients who present with this condition. The checklist is designed to optimize a patient's management in the first 24 hours when specialist liver/gastro input might not be available. Please arrange for a review of the patient by the gastro/liver team at the earliest opportunity. Escalation of care to higher level should be considered in patients not responding to treatment when reviewed after 6 hours, particularly in those with first presentation and those with good underlying performance status prior to the recent illness.

http://www.bsg.org.uk/care-bundles/care-bundles-general/index.html

McPherson S, Frontline Gastroenterology 2016

Case (2)

- Bloods
  - Hb 66
  - WCC 5.2
  - Platelets 75
  - PT 24 secs

  - Bilirubin 124
  - Albumin 28
  - ALT 25

  - Na 131
  - K 3.6
  - Urea 10.2
  - Creatinine 140

  - CRP 6

- Initial management
  - Fluid resuscitated with 1L N saline over 1 hour
  - X match 6 units blood
  - Transfused 2 units of blood
  - Given I.V Vitamin K 10mg stat
  - Stopped propranolol
  - Given 2mg terlipressin stat
  - Given 750mg Cefuroxime stat

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  - Hb 66
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- Initial management
  - Fluid resuscitated with 1L N saline over 1 hour
  - X match 6 units blood
  - Transfused 2 units of blood
  - Given I.V Vitamin K 10mg stat
  - Stopped propranolol and spironolactone
  - Gave 2mg terlipressin stat
  - Gave 750mg Cefuroxime stat
- 2 hours later
  - Pulse 70/min BP 115/62
  - Hb 75
  - Grade 2 encephalopathy
  - ITU/anaesthetic review
  - Endoscopy requested

Endoscopy

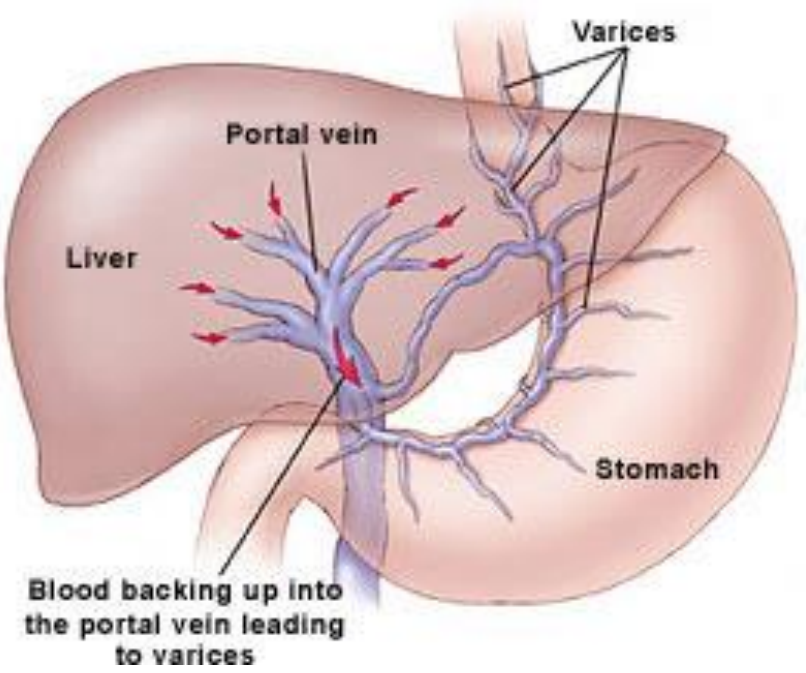
- Endotracheal intubation for endoscopy
- Actively bleeding varix just below GOJ
- 1 band place over bleeding point + 3 bands to lower oesophagus
- Bleeding stopped
- Patients sent to ITU overnight

How do varices develop and bleed?

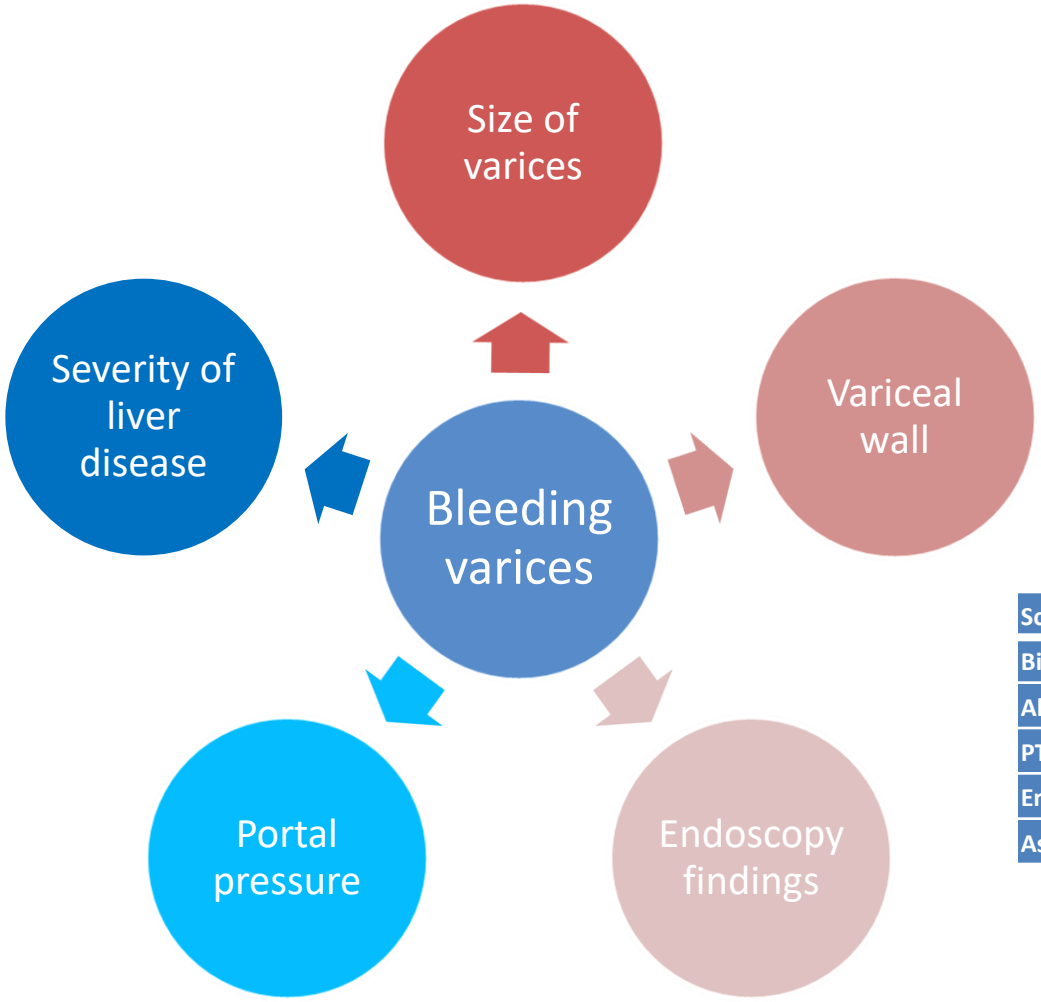
1. Liver resistance -> Increase portal pressure to above 12mmHg

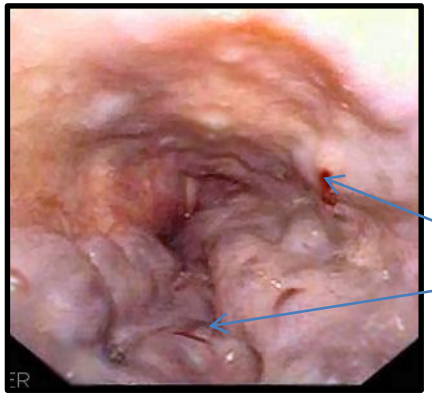
2. Collateral formation ->blood redirected to lower oesophagus, abdominal wall, stomach, rectum.

3. Small blood vessels become distended and thin walled



Risk factors for first bleed





Cherry red spots

Score	1	2	3
Bilirubin (micromol/l)	<34	34-50	>50
Albumin (g/l)	>35	28-35	<28
PT (s prolonged)	<4	4-6	>6
Encephalopathy	none	mild	marked
Ascites	none	mild	marked

Child Pugh score

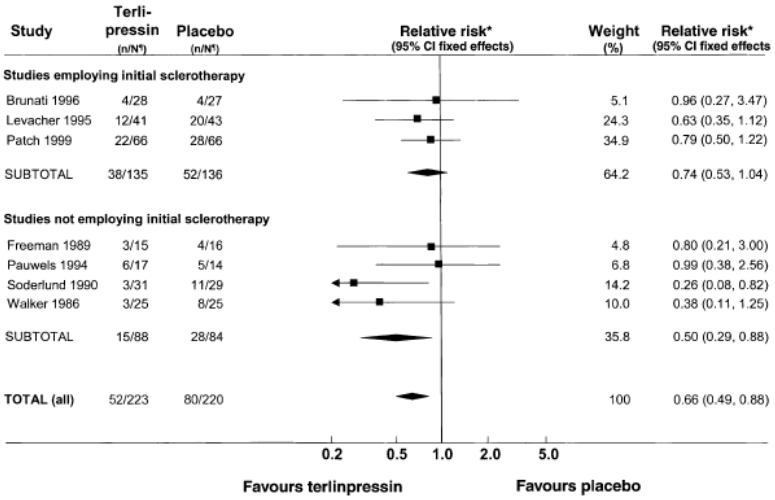
GI bleeding in cirrhotics – initial management

5. GI bleeding – if the patient has evidence of GI bleeding and varices are suspected		**N/A** ❑
a)	Fluid resuscitate according to BP, pulse and venous pressure	**Y N**
b)	Prescribe IV terlipressin 2mg four times daily (caution if known ischaemic heart disease or peripheral vascular disease)	**Y N NA**
c)	Prescribe prophylactic antibiotics as per Trust protocol (cefuroxime unless contraindicated)	**Y N**
d)	If prothrombin time (PT) prolonged give IV vitamin K 10mg stat	**Y N NA**
e)	If PT> 20 seconds (or INR >2.0) – give FFP (2-4 units)	**Y N NA**
f)	If platelets <50 – give IV platelets	**Y N NA**
g)	Transfuse blood if Hb <7.0g/L or massive bleeding (aim for Hb >8g/L)	**Y N NA**
h)	Early endoscopy **after** resuscitation (ideally within 12 hours)	**Y N**

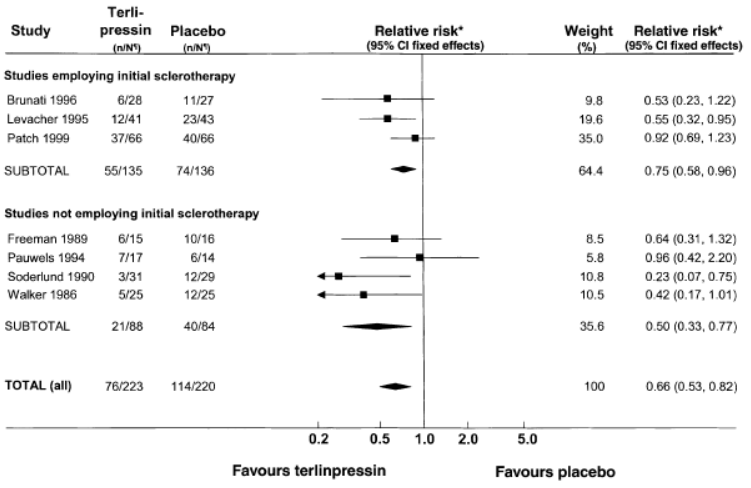
Remember it is the simple things that saves lives with GI bleeding not the endoscopy

Terlipressin for variceal bleeding

Reduces mortality



Improves control of bleeding



Vasoconstrictor drug that reduces portal pressure
Controls bleeding in 80% of bleeds

Ioannou G et el. Aliment Pharmacol Ther 2003 17 53-64

Antibiotics prevent infections in cirrhotic patients with GI bleeding

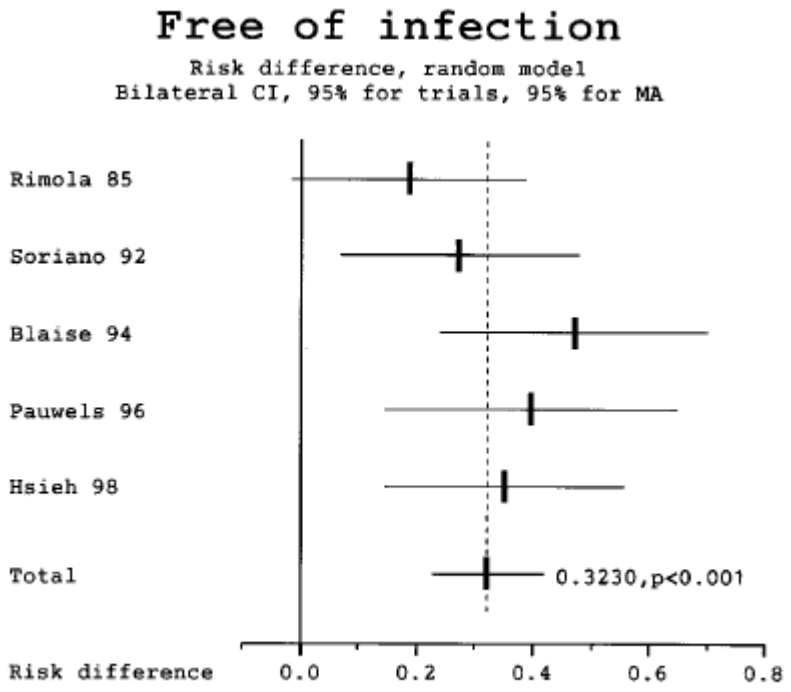


FIG. 1. Mean percentage of patients free of infection (Der Simonian).

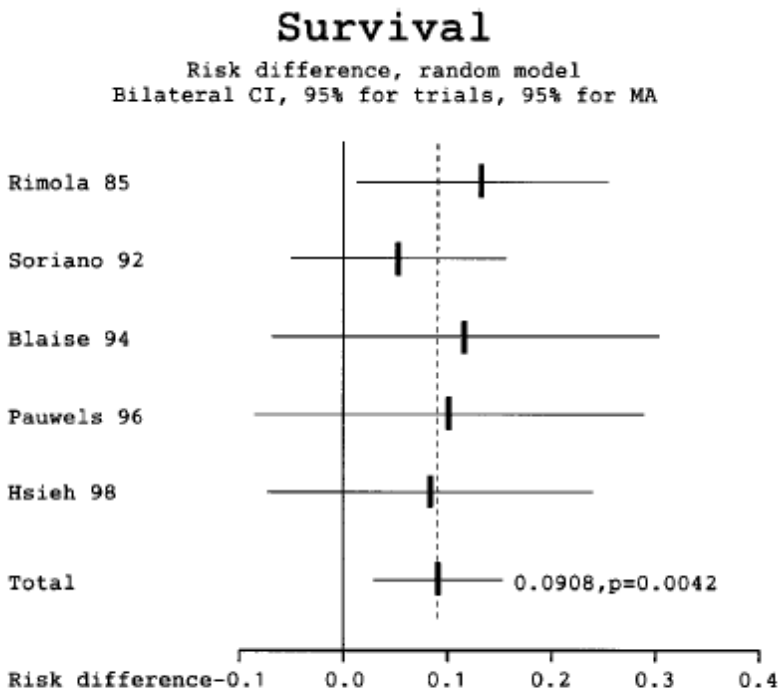
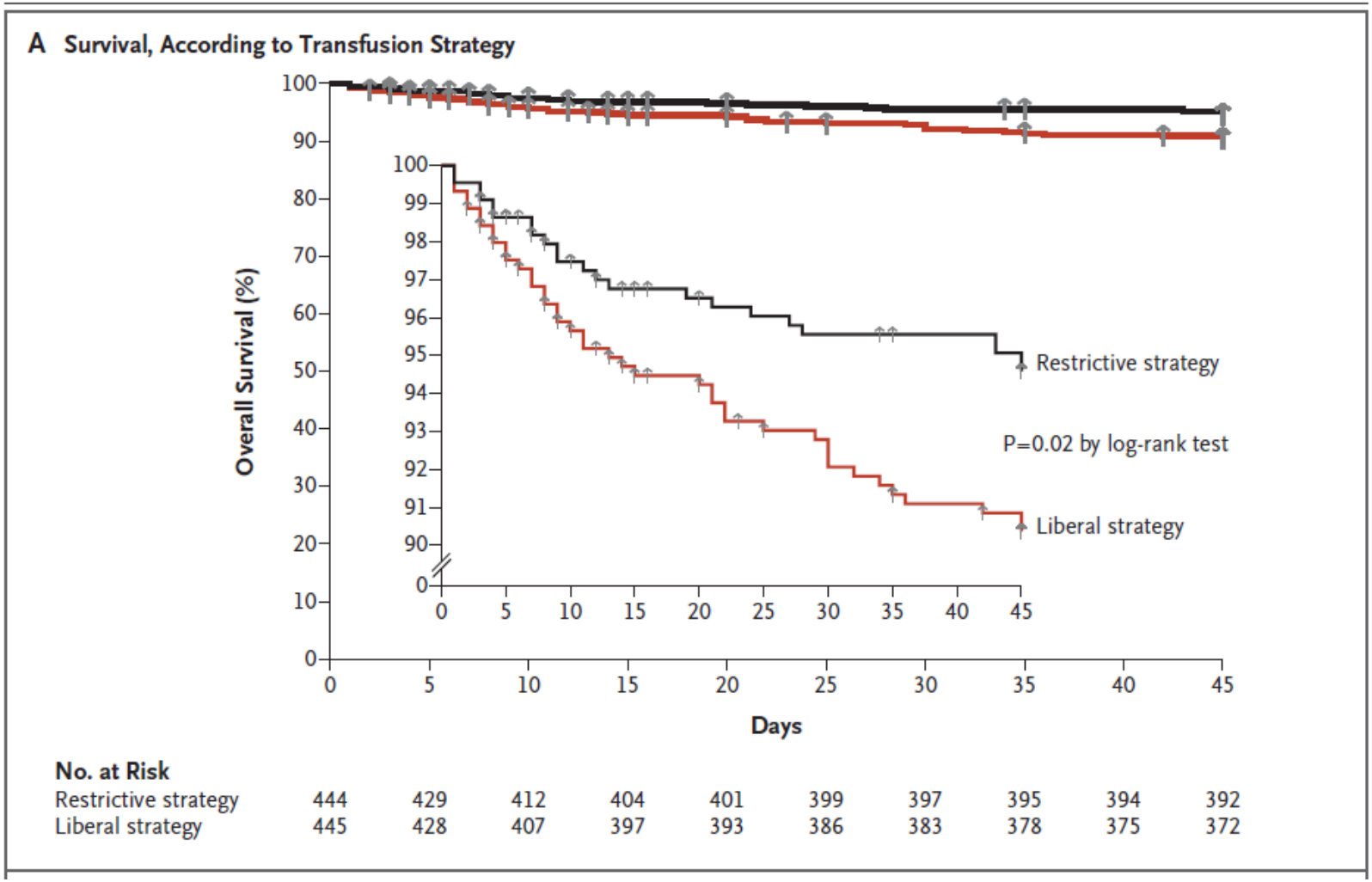


FIG. 4. Mean survival (Der Simonian).

Without prophylactic antibiotic 50% of patients with variceal bleed will develop a significant infection

Bernard et al. Hepatology 1999; 29: 1655-61

Restrictive transfusion strategy reduces mortality from GI bleeding

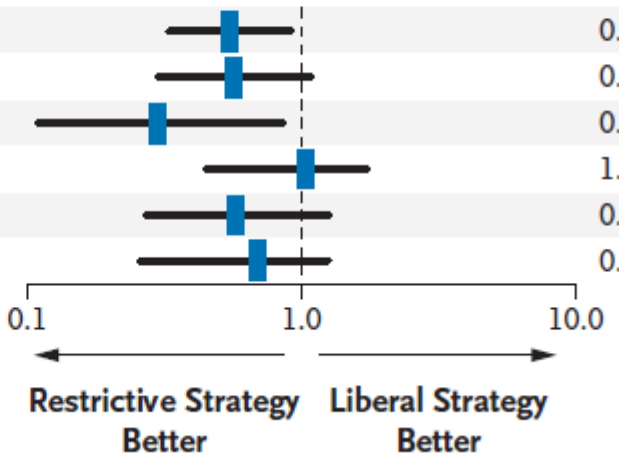


Villanueva C, N Engl J Med. 2013;368(1):11-21.

Restrictive transfusion strategy is effective in cirrhotics with GI bleeding

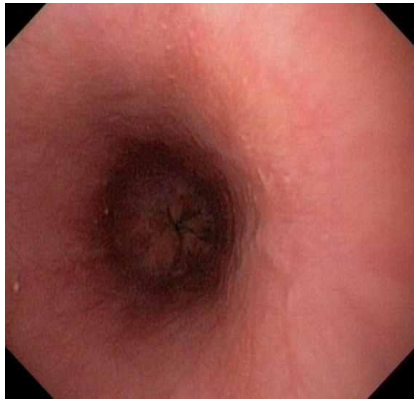
B Death by 6 Weeks, According to Subgroup

Subgroup	Restrictive Strategy	Liberal Strategy	Hazard Ratio (95% CI)	P Value
	no. of patients/total no. (%)			
Overall	23/444 (5)	41/445 (9)	0.55 (0.33–0.92)	0.02
Patients with cirrhosis	15/139 (11)	25/138 (18)	0.57 (0.30–1.08)	0.08
Child–Pugh class A or B	5/113 (4)	13/109 (12)	0.30 (0.11–0.85)	0.02
Child–Pugh class C	10/26 (38)	12/29 (41)	1.04 (0.45–2.37)	0.91
Bleeding from varices	10/93 (11)	17/97 (18)	0.58 (0.27–1.27)	0.18
Bleeding from peptic ulcer	7/228 (3)	11/209 (5)	0.70 (0.26–1.25)	0.26



Villanueva C, N Engl J Med. 2013;368(1):11-21.

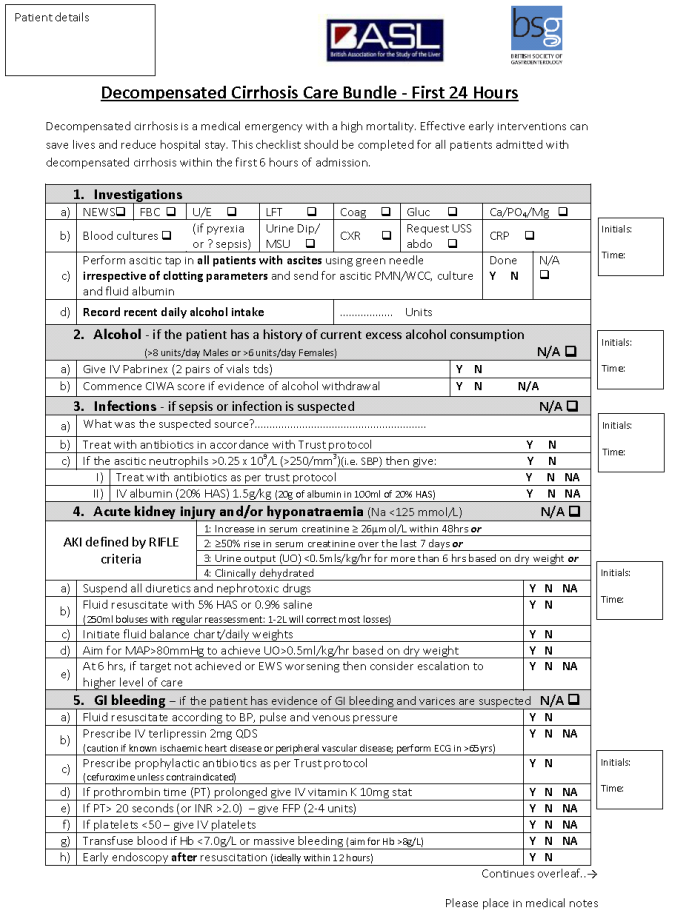
Banding of varices



Normal Oesophagus

Oesophageal varices

Remember to address all cirrhosis complications



Patient details

BASL — British Association for the Study of the Liver

bsg — British Society of Gastroenterology

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1. Investigations

a)	NEWS ❑	FBC ❑	U/E ❑	LFT ❑	Coag ❑	Gluc ❑	$Ca/PO_4/Mg$ ❑	
b)	Blood cultures ❑	(if pyrexia or ? sepsis)	Urine Dip/ MSU ❑	CXR ❑	Request USS abdo ❑	CRP ❑		Initials: Time:
c)	Perform ascitic tap in **all patients with ascites** using green needle **irrespective of clotting parameters** and send for ascitic PMN/WCC, culture and fluid albumin					Done Y N	N/A ❑	
d)	**Record recent daily alcohol intake** ..... Units							

2. Alcohol - if the patient has a history of current excess alcohol consumption (>8 units/day Males or >6 units/day Females) N/A ❑

a)	Give IV Pabrinex (2 pairs of vials tds)	Y N	Initials: Time:
b)	Commence CIWA score if evidence of alcohol withdrawal	Y N N/A	

3. Infections - if sepsis or infection is suspected N/A ❑

a)	What was the suspected source?.....		Initials: Time:
b)	Treat with antibiotics in accordance with Trust protocol	Y N	
c)	If the ascitic neutrophils >0.25 x 10^9/L (>250/mm^3)(i.e. SBP) then give:	Y N	
I)	Treat with antibiotics as per trust protocol	Y N NA	
II)	IV albumin (20% HAS) 1.5g/kg (20g of albumin in 100ml of 20% HAS)	Y N NA	

4. Acute kidney injury and/or hyponatraemia (Na <125 mmol/L) N/A ❑

AKI defined by RIFLE criteria	1: Increase in serum creatinine ≥ 26µmol/L within 48hrs ***or***	
	2: ≥50% rise in serum creatinine over the last 7 days ***or***	
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	4: Clinically dehydrated	
a)	Suspend all diuretics and nephrotoxic drugs	Y N NA
b)	Fluid resuscitate with 5% HAS or 0.9% saline (250ml boluses with regular reassessment: 1-2L will correct most losses)	Y N
c)	Initiate fluid balance chart/daily weights	Y N
d)	Aim for MAP>80mmHg to achieve UO>0.5ml/kg/hr based on dry weight	Y N
e)	At 6 hrs, if target not achieved or EWS worsening then consider escalation to higher level of care	Y N NA

Initials: Time:

5. GI bleeding – if the patient has evidence of GI bleeding and varices are suspected N/A ❑

a)	Fluid resuscitate according to BP, pulse and venous pressure	Y N
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Initials: Time:

Continues overleaf...→

Please place in medical notes

6. Encephalopathy N/A ❑

a)	Look for precipitant (GI bleed, constipation, dehydration, sepsis etc.)	Y N
b)	Encephalopathy – lactulose 20-30ml QDS or phosphate enema (aiming for 2 soft stools/day)	Y N
c)	If in clinical doubt in a confused patient request CT head to exclude subdural haematoma	Y N N/A

Initials: Time:

7. Other

a)	Venous thromboembolism prophylaxis – prescribe prophylactic LMWH (patients with liver disease are at a high risk of thromboembolism even with a prolonged prothrombin time; withhold if patient is actively bleeding or platelets <50)	Y N NA
b)	GI/Liver review at earliest opportunity (ideally within 24 hrs)	❑

Initials: Time:

Name.....Grade.....Date.....Time.....

Decompensated Cirrhosis Care Bundle - First 24 Hours

The recent NCEPOD report 2013 on alcohol related liver disease highlighted that the management of some patients admitted with decompensated cirrhosis in the UK was suboptimal. Admission with decompensated cirrhosis is a common medical presentation and carries a high mortality (10-20% in hospital mortality). Early intervention with evidence-based treatments for patients with the complications of cirrhosis can save lives. This checklist aims to provide a guide to help ensure that the necessary early investigations are completed in a timely manner and appropriate treatments are given at the earliest opportunity.

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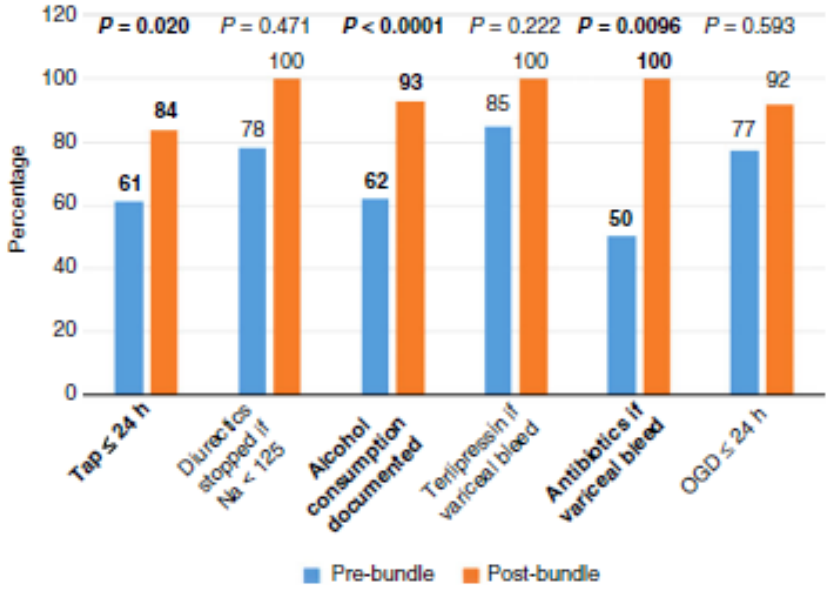
http://www.nescn.nhs.uk/wp-content/uploads/2014/05/Cirrhosis-Care-Bundle.pdf

Use of a care bundle improves the care of cirrhotic patients presenting with GI bleeding

- Outcomes of implementation assessed in 3 hospitals
  - Newcastle
  - Sunderland
  - Royal Cornwall Hospital
- 228 patients with decompensated cirrhosis reviewed
- High level of usage of the care bundle
  - Increased to 90% in Newcastle
- Improvement in all aspects addressed in the Bundle
- Hospital stay reduced from 11 days to 8 days

Table 2 | Primary reason for admission to hospital

Clinical reason for hospital admission	Percentage of cohort
Ascites	34
Hepatic encephalopathy	20
Upper gastrointestinal bleeding	20
Jaundice	15
Sepsis	5
Other	6



Dyson J et al Alimentary Pharmacology and Therapeutics Oct 2016

Should cirrhotics with GI bleeding go to ITU?

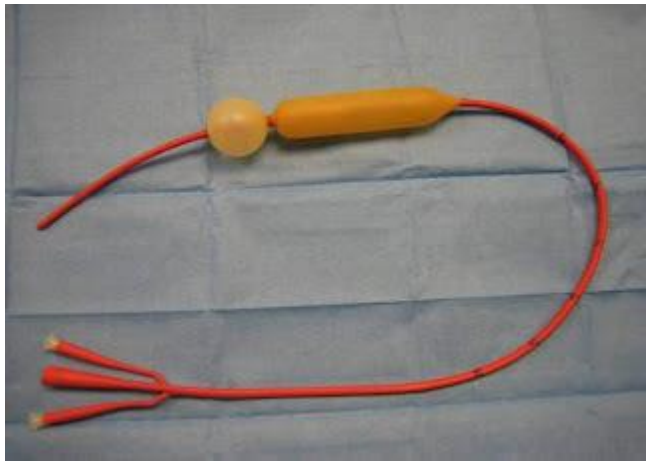
		Survivors	Non-survivors	p value
Number		307 (55%)	256 (45%)	-
Age		49 (30-68)	51 (34-68)	ns
Male : Female		196:111	152:104	ns
Aetiology	Alcohol	146/263 (56%)	117/263 (44%)	ns
	Other	161/300 (54%)	139/300 (46%)	
Reason for Admission	Variceal Bleed	139/196 (71%)	57/196 (29%)	<0.0001
	Non Variceal	168/367 (46%)	199/367 (54%)	

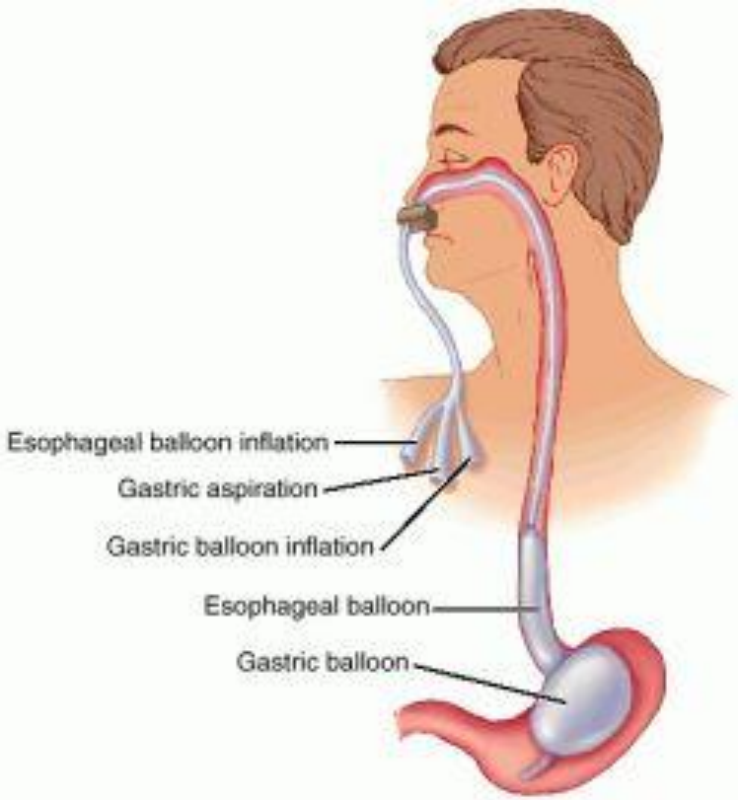
Cholongitas E et al J Gastroenterol Hepatol. 2008;23:1223-7

Back to the case

- Stayed on ITU overnight extubated the next morning
- No further bleeding for 24 hours
- Continued medical treatments
- Remained stable so sent to Liver ward
- On day 3 further large haematemesis with haemodynamic instability
- Reintubated and had repeat endoscopy
- Endoscopy showed uncontrollable bleeding from the lower oesophagus

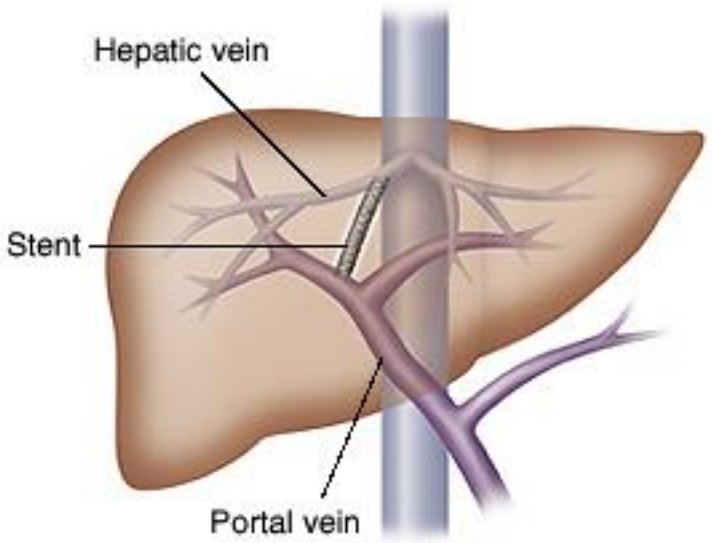
Minnesota tube placed





TIPSS

- Shunt between portal and hepatic vein – rapid reduction in portal pressure
- Very effective treatment for oesophageal and gastric variceal bleeding (and refractory ascites)
- Significant risks from encephalopathy, liver failure and infection
- Careful patient selection required



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Early Use of TIPS in Patients with Cirrhosis and Variceal Bleeding

Juan Carlos García-Pagán, M.D., Karel Caca, M.D., Christophe Bureau, M.D., Wim Laleman, M.D., Beate Appenrodt, M.D., Angelo Luca, M.D., Juan G. Abraldes, M.D., Frederik Nevens, M.D., Jean Pierre Vinel, M.D., Joachim Mössner, M.D., and Jaime Bosch, M.D., for the Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group

63 patients

Child's B with active bleeding or Child's C

Randomized to standard therapy or early TIPSS

Primary endpoint – rebleeding or failure to control bleeding

Secondary endpoint - survival

Rebleeding rates

Survival

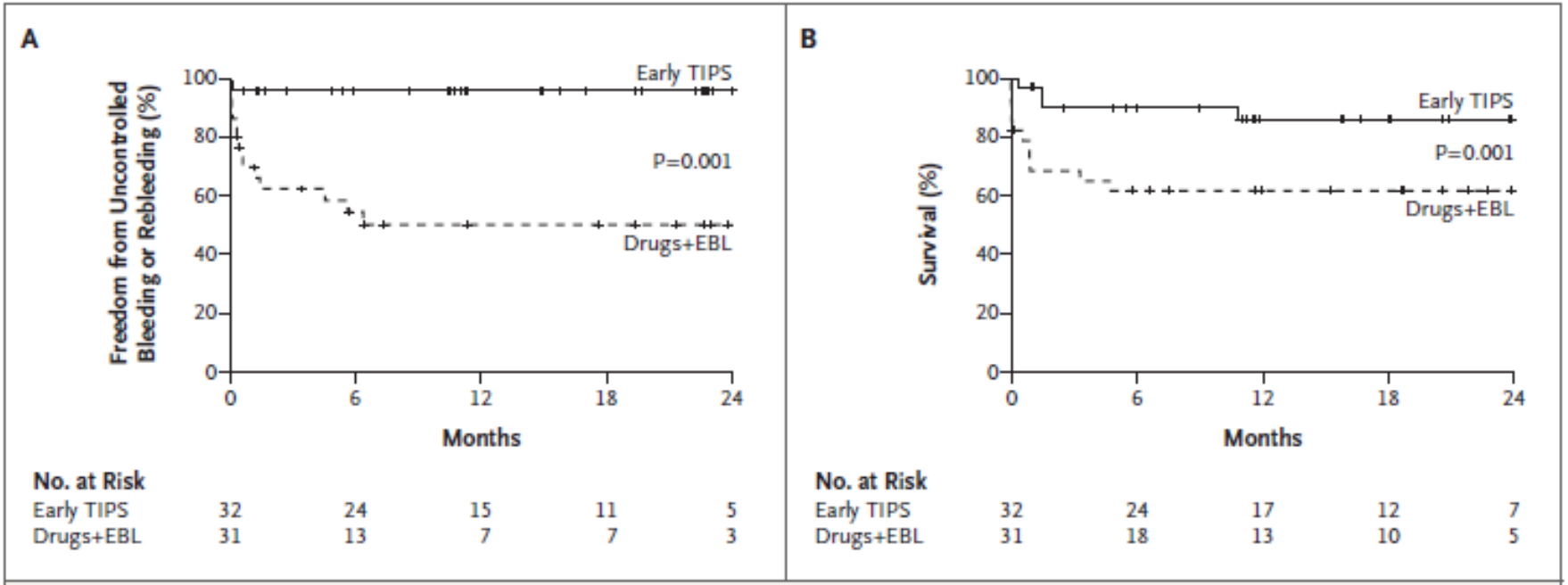
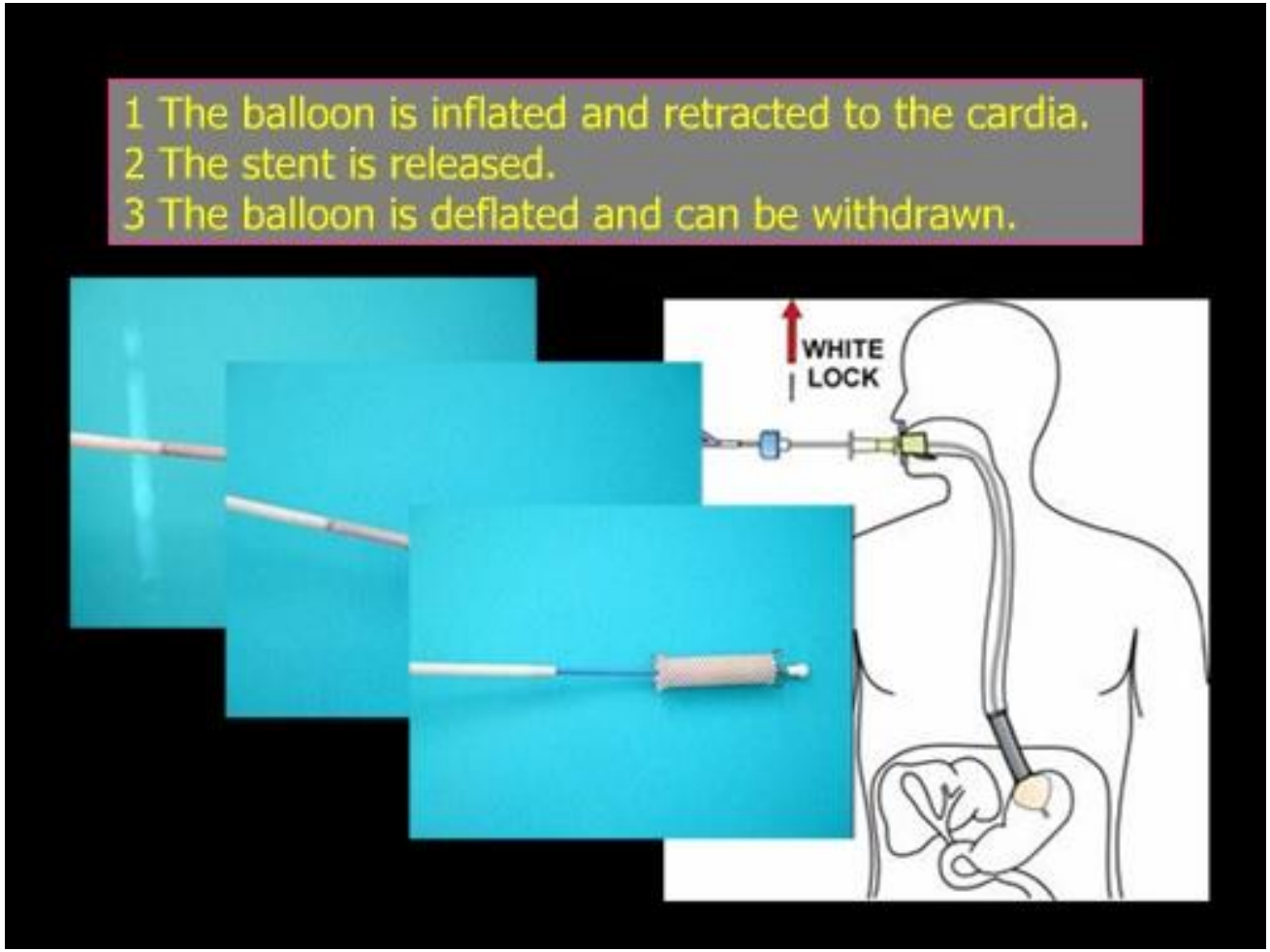


Figure 2. Actuarial Probability of the Primary Composite End Point and of Survival, According to Treatment Group.

The probability of remaining free from uncontrolled variceal bleeding or variceal rebleeding is shown in Panel A, and the probability of survival is shown in Panel B. EBL denotes endoscopic band ligation, and TIPS transjugular intrahepatic portosystemic shunt.

Self expanding metal stents

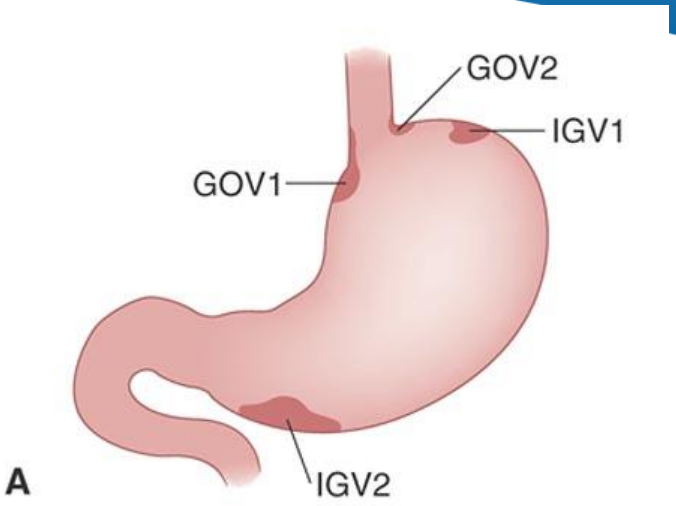


Case

- TIPPS placed. HVPG 21mmHg – reduced to 12 mmHg
- 5 days on ICU with AKI and encephopathy – slow to wake up
- Further 7 days on ward with gradual improvement in Liver function + AKI
- Discharged home – Stopped drinking!!
- Remains under follow up

Gastric varices

- Present in 20% of cirrhotics at first endoscopy
- Bleed at lower pressure the oesophageal varices
- Worse outcomes then oesophageal varices
- With isolated gastric varices consider extra-hepatic portal hypertension due to splenic vein thrombosis

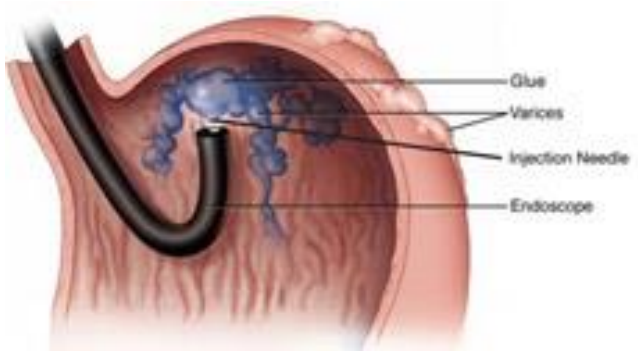


Gastric varices - options

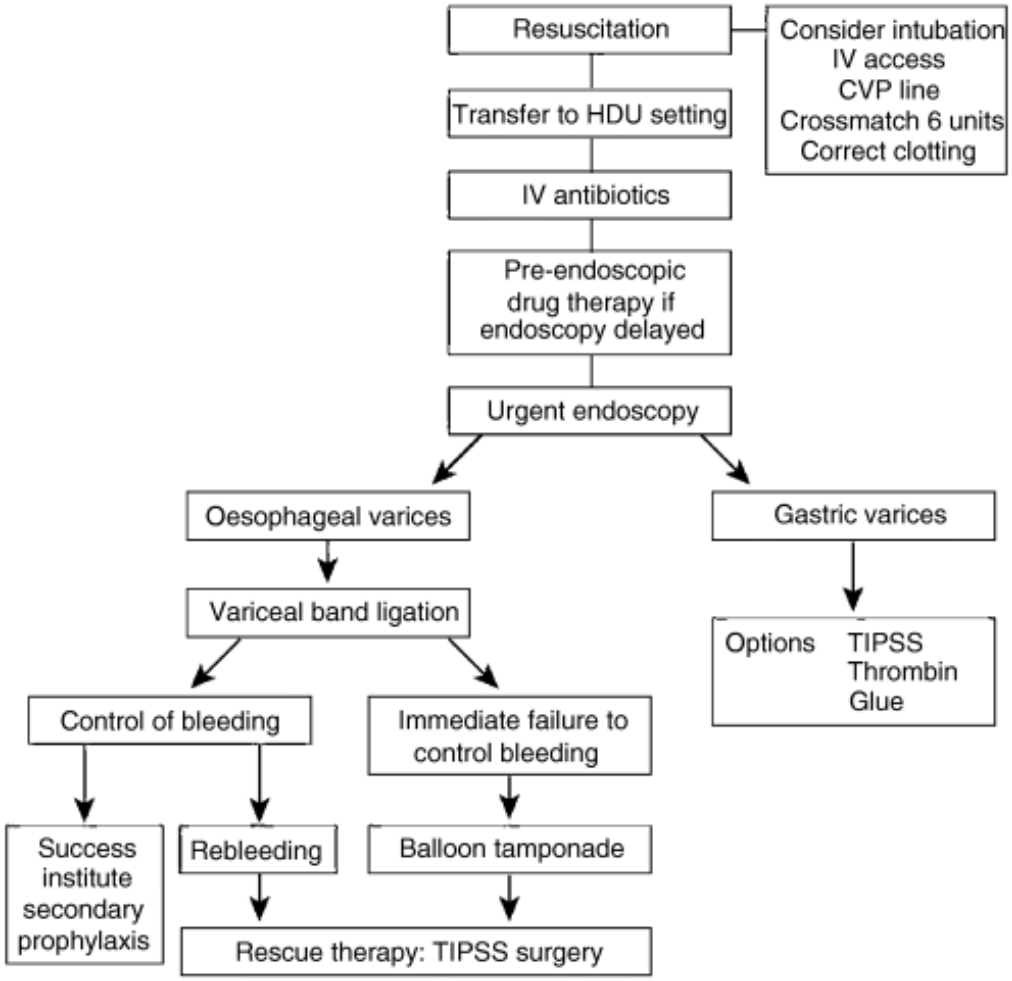
- Endoscopic
  - 'Superglue' : cyanoacrylate
    - Better control compared with banding (87% vs 45%)
    - reduced mortality (29% vs 48%)
    - Lower re-bleeding (31% vs 54%)
  - Thrombin
    - Higher rebleeding rates than Glue
- Radiological
  - TIPSS
  - Balloon occluded retrograde transvenous obliteration (BRTO) for IGV-1
- Primary prevention
  - Beta blockers better than no treatment

Lo GH Hepatology 2001 33 1060-4
Mishra SR Hepatology 2011 54 1161

Gluing of varices



Management of acute variceal bleeding



Prevention of re-bleeding

- After an episode of variceal bleeding it is important to try and reduce risk of further bleeding
- Patients should enter variceal obliteration program
- Commence non-cardioselective beta blocker
  - Carvedilol should now be first line
  - Reduces portal pressure more effectively than propranolol
  - Start 3.125mgBD – increasing to 6.25mgBD
  - Aim HR ≤60/min and SBP >100 mmHg
- Abstinence from alcohol

Take home messages – Variceal bleeding

- Early resuscitation saves lives
- Airway protection very important in large bleeds or encephalopathy
- Give antibiotics and terlipressin early
- Early endoscopy **after** resuscitation
- Don’t forget all the other aspects of care- AKI, infections, alcohol withdrawal etc. Care bundle can help with this