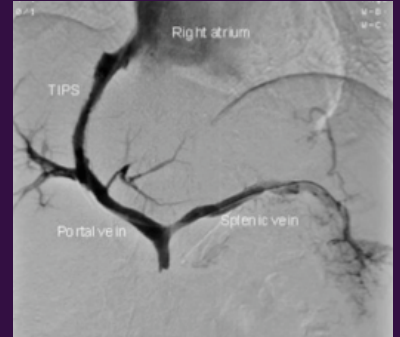
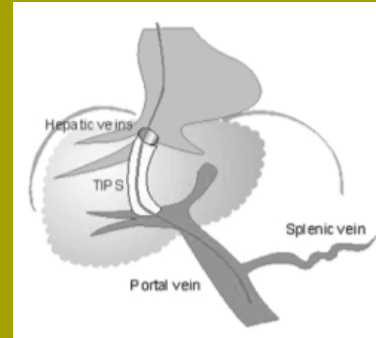




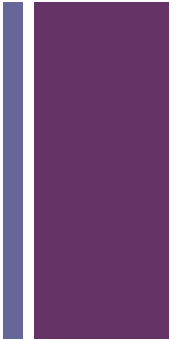
Anju Sidhu MD
University of Louisville
Gastroenterology, Hepatology and Nutrition
February 16, 2012



A TALK ABOUT TIPS



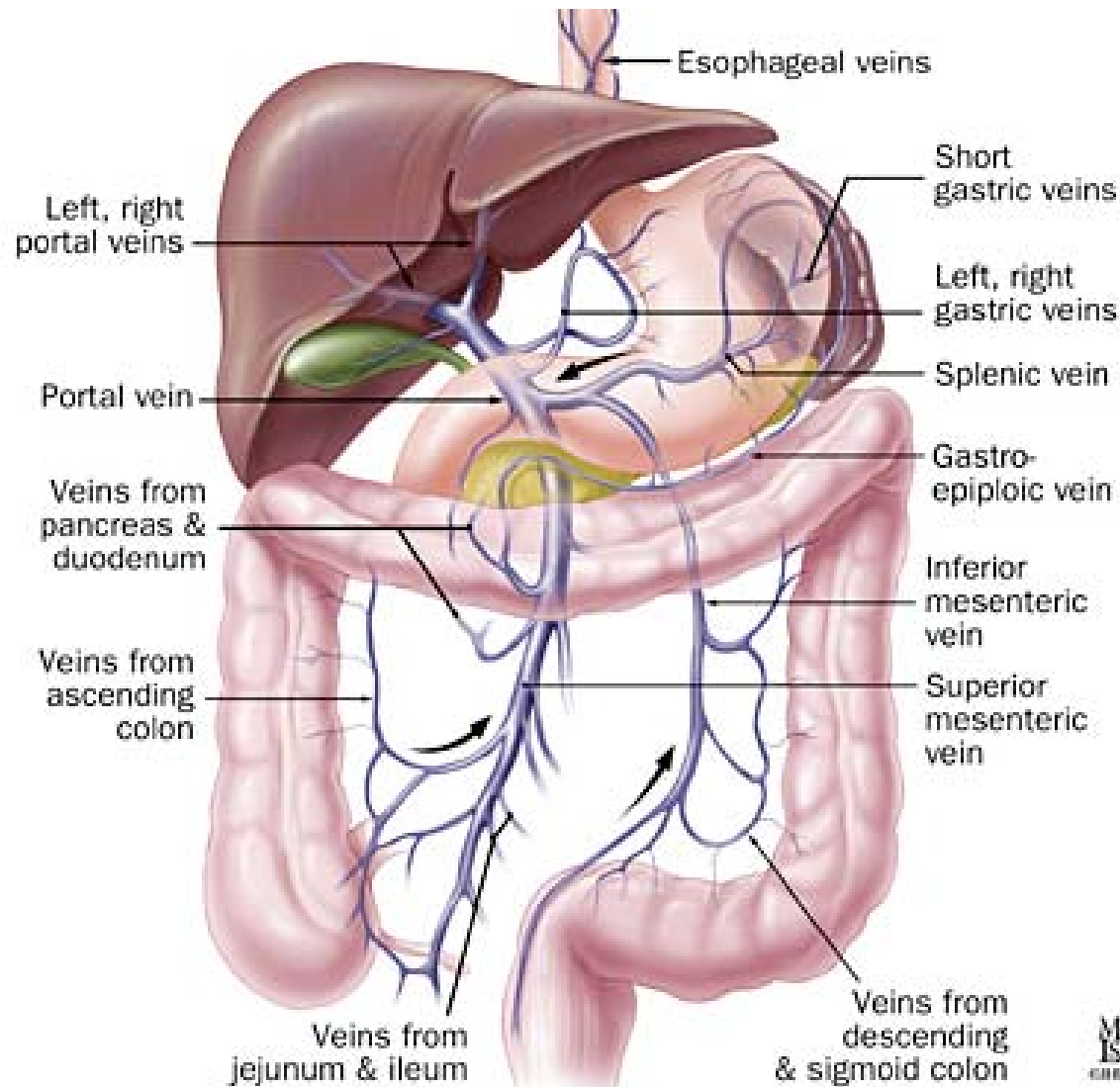
Overview



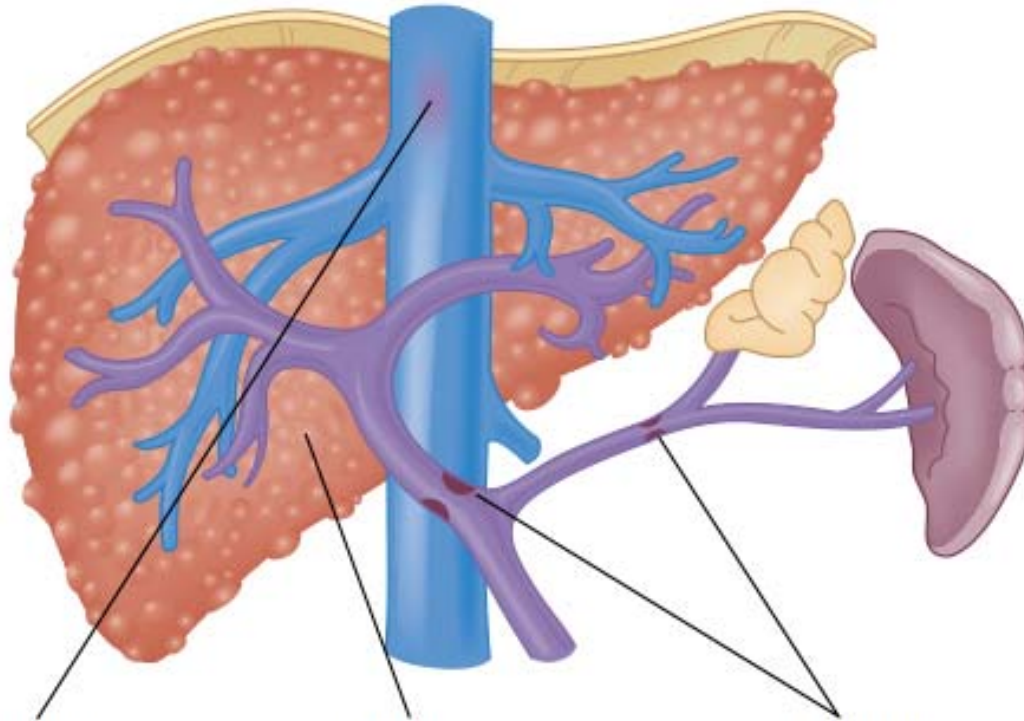
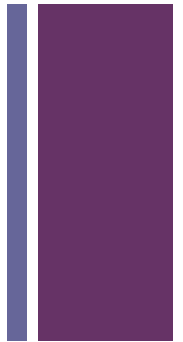
- Anatomy and Portal HTN
- The Procedure
- Complications
- Indications (and Contraindications)



Portal Vasculature



+ Portal Hypertension



Posthepatic

Budd-Chiari syndrome
Constrictive pericarditis
Inferior vena caval obstruction
Right-sided heart failure
Severe tricuspid regurgitation

Intrahepatic

Presinusoidal

Idiopathic portal hypertension
Primary biliary cirrhosis
Sarcoidosis
Schistosomiasis

Sinusoidal

Alcoholic cirrhosis
Alcoholic hepatitis
Cryptogenic cirrhosis
Postnecrotic cirrhosis

Postsinusoidal

Sinusoidal obstruction syndrome

Prehepatic

Portal vein thrombosis
Splenic vein thrombosis

--Changes in
Portal
Resistance

--Changes in
Portal Flow

+ Portal Pressure

NORMAL = 5-10mmg Hg

■ DIRECT MEASUREMENT

- Invasive, cumbersome, infrequently done

■ INDIRECT MEASUREMENT

- Splenic pulp pressure (yikes! bleeding. . .)

- Hepatic Venous Pressure Gradient (HVPG) = FREE HV PRESSURE – WEDGED HV PRESSURE

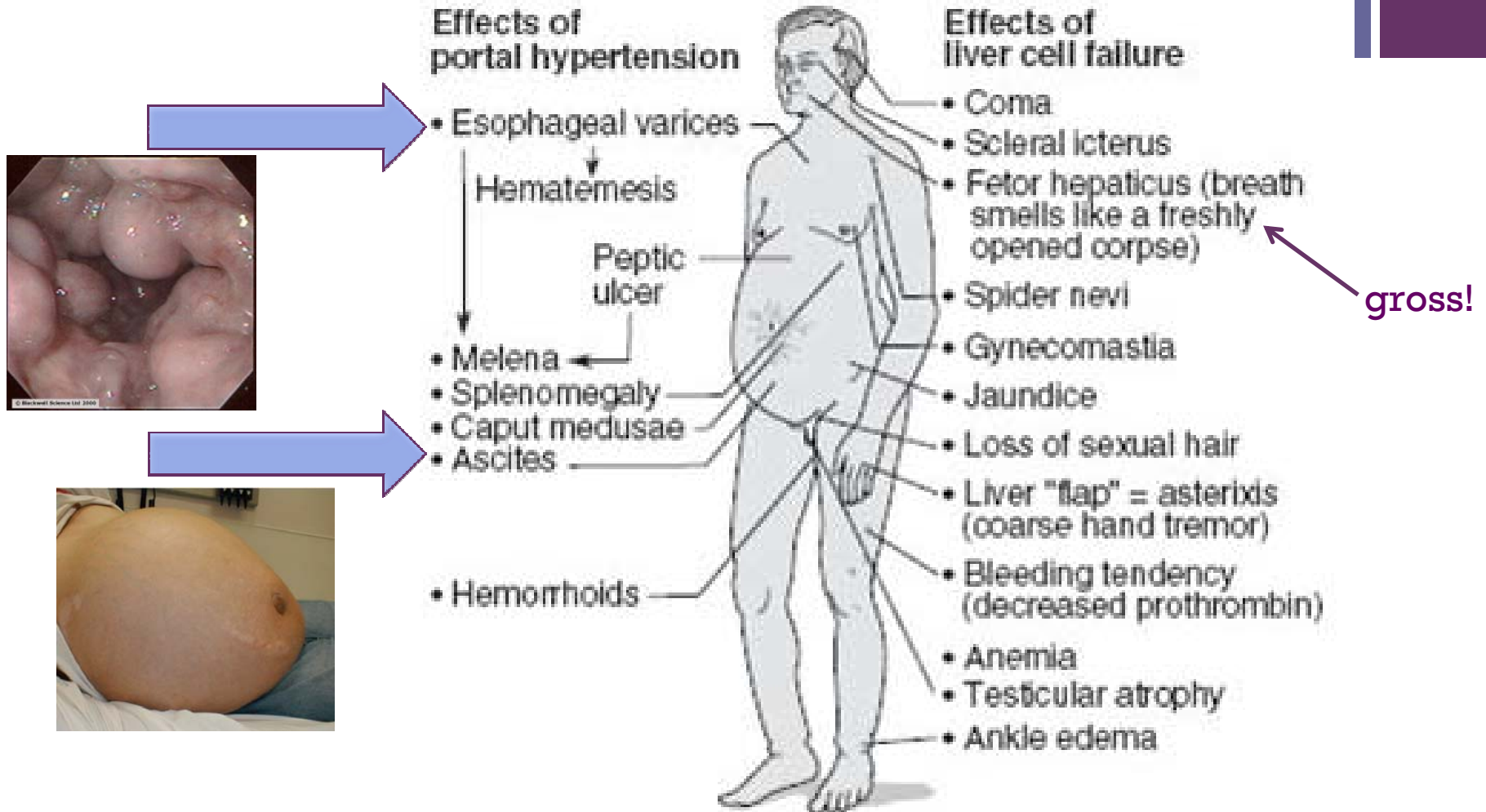
Table 90-1 The Use of Hepatic Venous Pressure Gradient in the Differential Diagnosis of Portal Hypertension

TYPE OF PORTAL HYPERTENSION	WHVP	FHVP	HVPG
Prehepatic	Normal	Normal	Normal
Presinusoidal	Normal	Normal	Normal
Sinusoidal ←	Increased	Normal	Increased
Postsinusoidal	Increased	Normal	Increased
Posthepatic			
Heart failure	Increased	Increased	Normal
Budd-Chiari syndrome	—	Hepatic vein cannot be cannulated	—

FHVP, free hepatic vein pressure; HVPG, hepatic venous pressure gradient; WHVP, wedged hepatic venous pressure.

+

Complications of Portal HTN



[Random Internet Pictures]

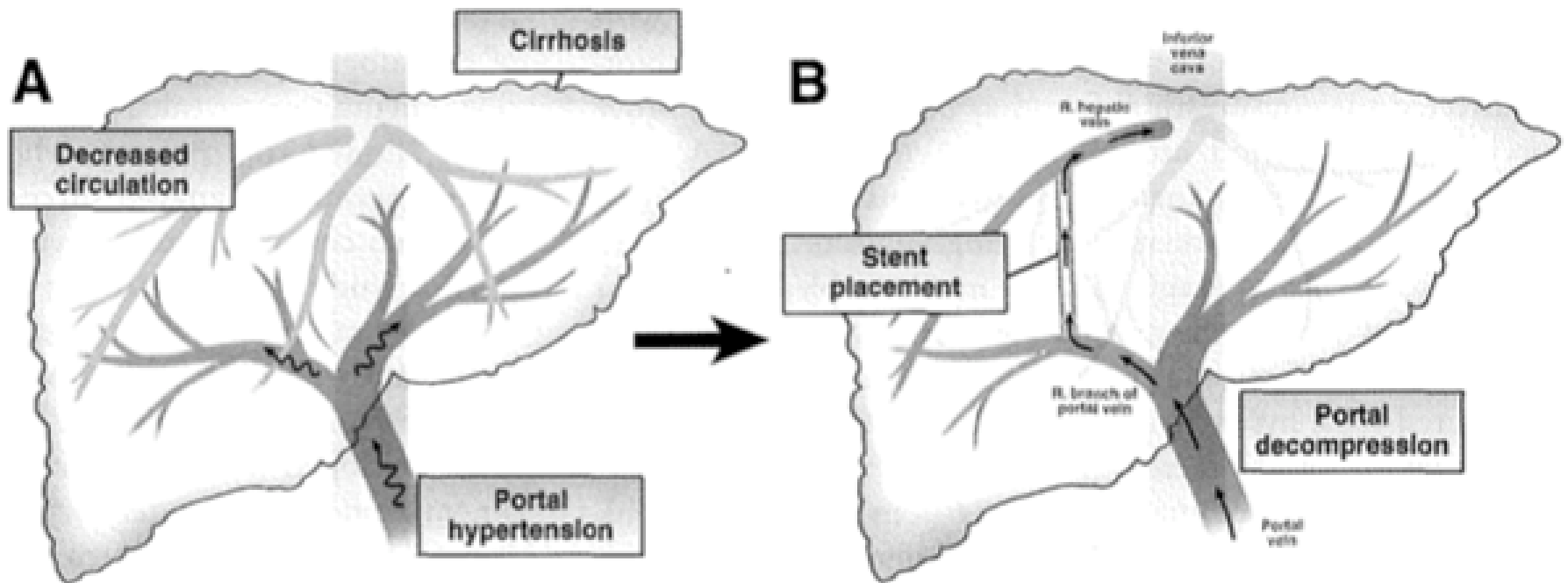
+ Origins of TIPS





Illustration

Transjugular Intrahepatic Portosystemic Shunt



+ TIPS Creation

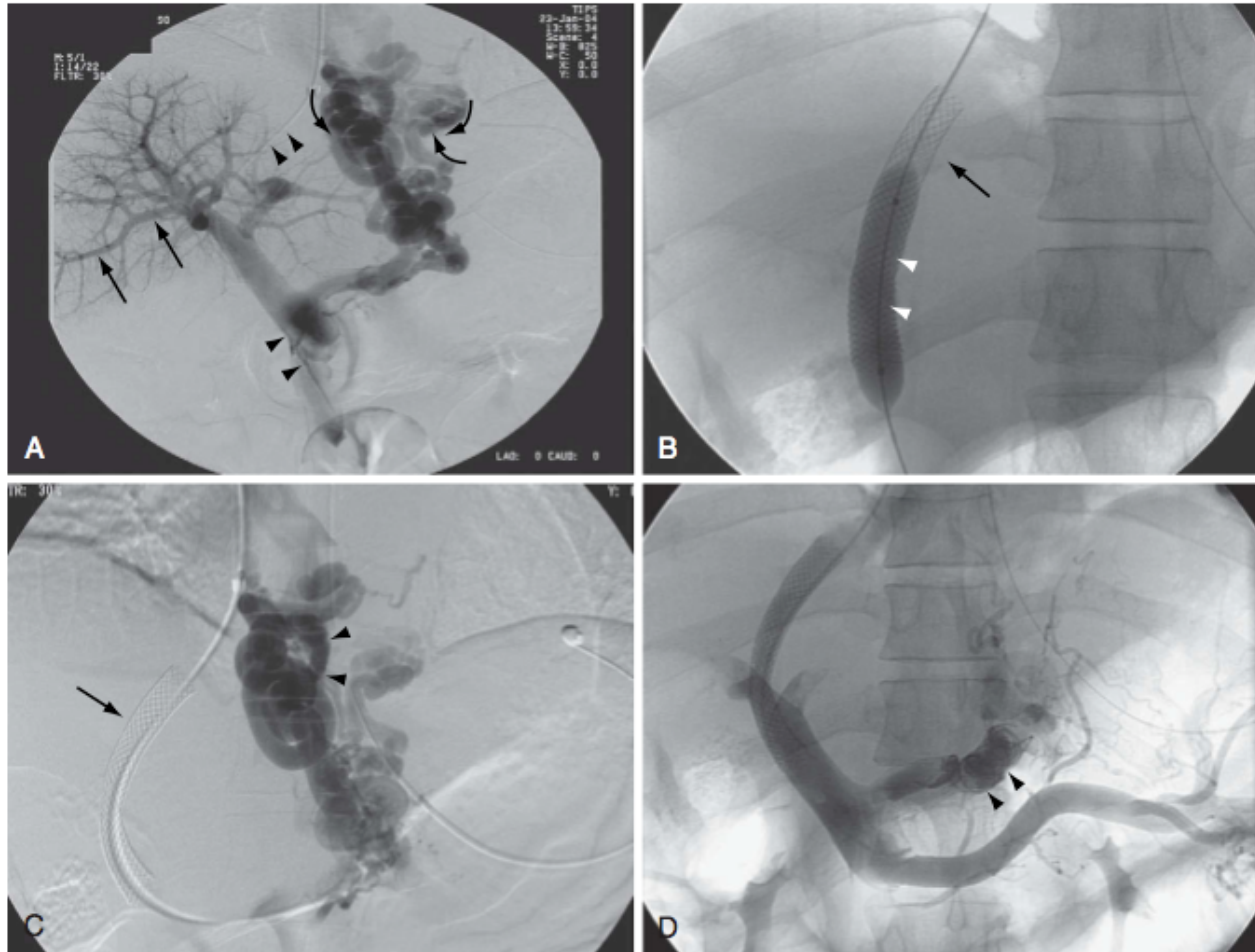


Figure 90-10. Creation of a transjugular intrahepatic portosystemic shunt (TIPS). A, Portogram with a catheter in the portal venous system (*arrowheads*). The portal venous system is clearly outlined (*straight arrows*). Gastroesophageal collaterals are also demonstrated (*curved arrows*). B, A stent (*arrow*) has been placed to bridge the hepatic vein and the portal vein. A balloon (*arrowheads*) is being used to dilate the parenchymal tract within the liver. C, Following expansion of the stent (*arrow*), injection into the portal vein demonstrates persistence of the gastroesophageal varices (*arrowheads*). D, Following embolization of the varices with steel coils (*arrowheads*), the intrahepatic portal vasculature is no longer demonstrated, indicative of hepatofugal flow of portal blood through the shunt.

+ Stents: Coated (not Uncoated)

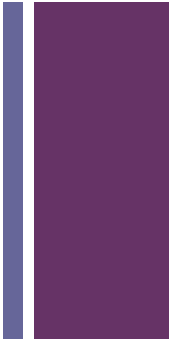


Gore Viatorr Stents
Being used at JH and UL.



Figure 2. Explanted liver of a patient treated by TIPS 7 months before, showing the intrahepatic portion of the prosthesis covered with PTFE and the bare portion in the portal stem. A radiopaque marker (arrow) demarcates the 2 portions.

+ Patient Preparation



- The right patient
- Doppler U/S to document patency of PV
- Consider 2D echo with bubble study
 - to evaluate for pulmonary HTN
- Antibiotic prophylaxis
 - Is standard of care,
though does not decrease peri-procedural infection



Complications

■ TECHNICAL - ACCESS

- Carotid artery puncture
- Tracheal puncture
- Extrahepatic PV puncture
- Capsule Traversal (common)
 - Hemoperitoneum (rare)
- Arrhythmias!!
 - Watch out if pt has LBBB, if you add a RBBB = complete heart block ☹️

■ TECHNICAL - STENT

- Thrombosis/Occlusion
- Migration
- Fistula

Pseudointimal
Hyperplasia

■ SHUNTING

- PSE
- Hemodynamic consequences
- Sepsis

■ OTHER

- Hemolytic anemia
(rule out Zieve's syndrome)
- **Hyperbilirubinemia**
- Vegetative infections

Bad News!

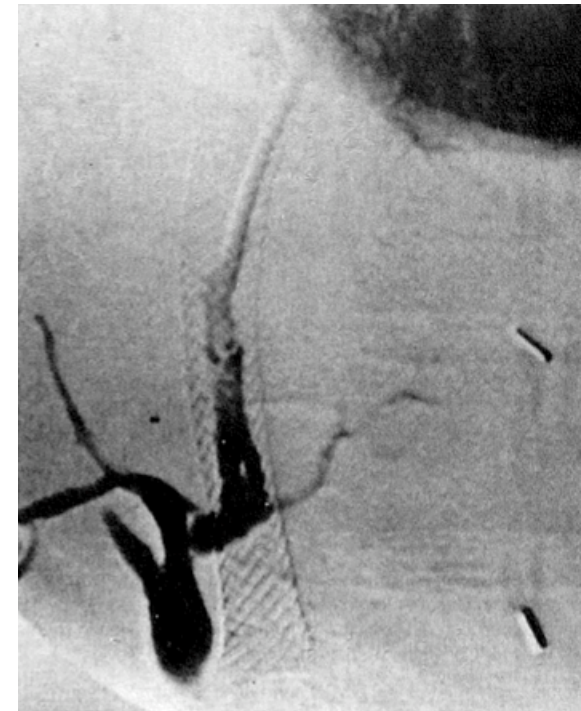


Complication Frequency

Table 3. Complications of TIPS

Complications	Frequency (%)
TIPS dysfunction ←	
Thrombosis	10-15
Occlusion/stenosis	18-78
Transcapsular puncture	33
Intraperitoneal bleed	1-2
Hepatic infarction	~1
Fistulae	Rare
Hemobilia	<5
Sepsis	2-10
Infection of TIPS	Rare
Hemolysis	10-15
Encephalopathy ←	
New/worse	10-44
Chronic	5-20
Stent migration or placement into IVC or too far into portal vein	10-20

Data from Boyer and Vargus¹²⁶ and Rössle et al.¹²⁷



**STENT-BILIARY
FISTULA**

[Freedman Radiographics]



Coated vs. Uncoated Stents?

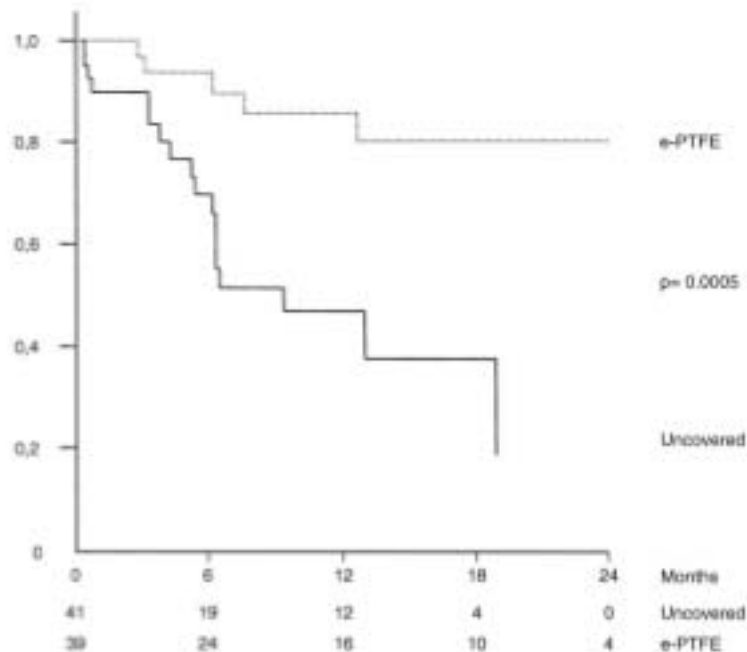


Figure 3. Probability of remaining free of shunt dysfunction after the TIPS procedure in the 2 groups. Numbers below the graph are patients at risk at each time point.

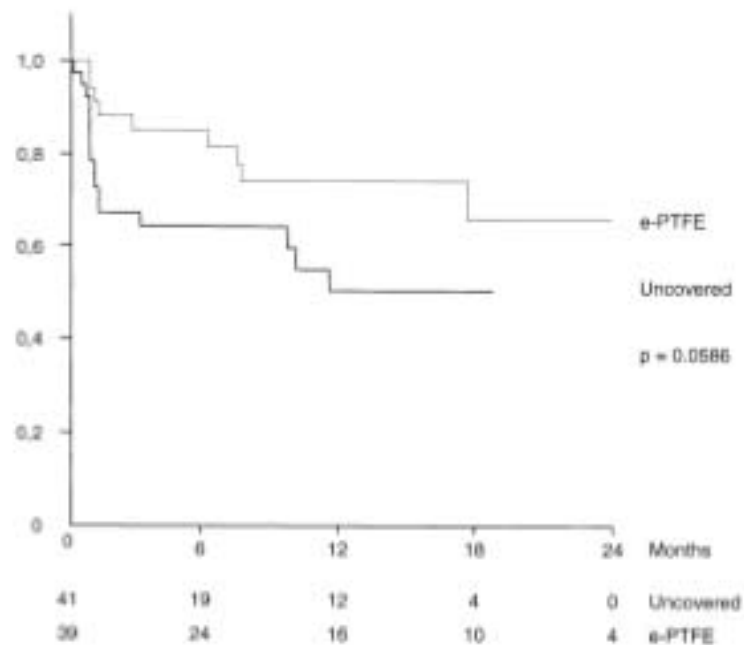


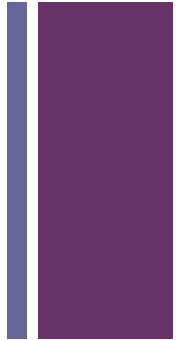
Figure 4. Probability of remaining free of encephalopathy after the TIPS procedure in the 2 groups. Numbers below the graph are patients at risk at each time point.

Definitely Coated!

[Bureau Gastroenterology 2004]

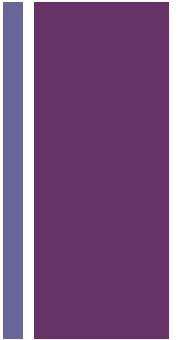


Successful TIPS Placement



- Society of Interventional Radiology Guidelines
 - Technical: Creation of a patent TIPS
 - Hemodynamic: Decrease in portal pressure to **<12mmHg**
 - Clinical: Resolution of indication for which it was performed
- Success Rate >90%

SO THE BIGGEST
QUESTION IS:
WHO DO YOU TIPS?



- REFRACTORY CIRRHOTIC ASCITES
- SECONDARY PREVENTION OF VARICEAL BLEED
 - Refractory Acute Variceal Bleed
 - Bleeding Gastric Varices
 - Portal HTN Gastropathy
 - Budd-Chiari Syndrome
 - Refractory Hepatic Hydrothorax



UNCLEAR EFFICACY

Last
ditch
effort!

- ■ Hepatorenal Syndrome
- Hepatopulmonary Syndrome

NO EFFICACY

- Veno-Occlusive Disorder (SOS)
- GAVE




+ Contraindications

ABSOLUTE

- Primary prevention of VB
- Acute CHF
- Multiple hepatic cysts
- Uncontrolled sepsis/infection
- Unrelieved biliary obstruction
- Severe pulmonary HTN

RELATIVE

- Portal vein thrombus
- Severe coagulopathy (INR>5)
- Severe thrombocytopenia (<20K)
- Moderate pulmonary HTN
- Advanced liver disease? 
(stay tuned,
more to come. . .)

+ What is Refractory Ascites?

Ascites that cannot be mobilized or early recurrence because. . .

- DIURETIC-INTRACTABLE ASCITES = REFRACTORY

└ Lack of response to Na restriction and diuretic treatment

- DIURETIC-RESISTANT ASCITES = RECIDIVANT

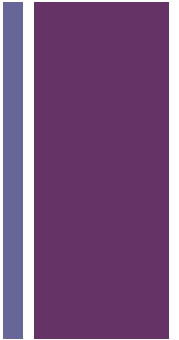
└ Development of diuretic-induced complications

REQUIRES:

- 1) Spironolactone 400mg/day and furosemide 40mg/day, 90mmol/day salt-restriction
- 2) Diuretics for at least a week
- 3) Reappearance of ascites within 4 weeks of mobilization
- 4) Diuretic-induced complications



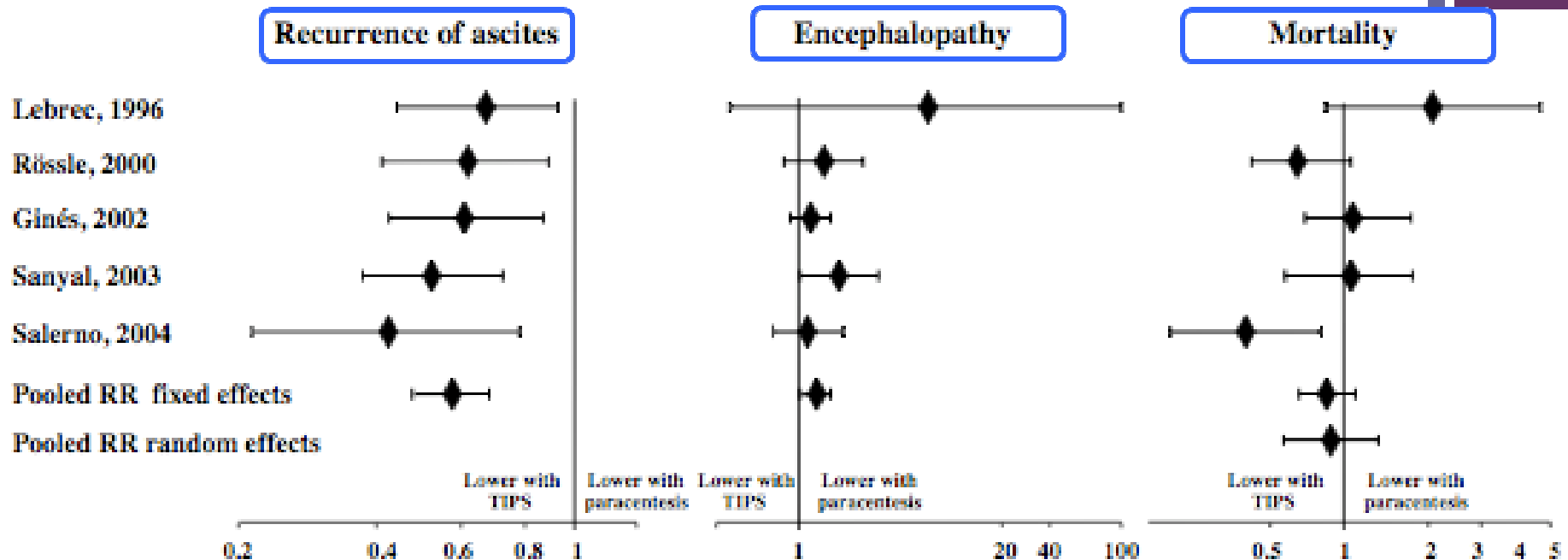
TIPS for Refractory Ascites



■ **EASL GUIDELINES**

- Effective in management of refractory ascites but
 - Associated with increased risk of HE
 - Not convincingly shown to improve survival
 - *compared to repeated LVPs
- Consider in those requiring very frequent LVPs or those with loculated ascites

+ Meta-Analysis: LVPs vs. TIPS



SIMPLE SUMMARY:
TIPS improves ascites,
worsens HE,
no effect on survival
(Fine print on next slide. . .)

[Albilos 2005]

+ Meta-Analysis: LVPs vs. TIPS in more detail. . .

Author, year (Ref)	n	2-year survival (%)		p Value
		TIPS	Paracentesis	
Lebrec 1996 ²⁹	25	29	60	0.03
Rössle 2000 ⁵⁸	60	58	32	0.02
Gines 2002 ⁸⁶	70	26	30	0.51
Sanyal 2003 ⁵²	109	62	62	NS
Salerno 2004 ⁸⁷	66	79	29	0.021

Author, year (Ref)	Bilirubin (mg/dl)	Creatinine (mg/dl)
Lebrec 1996 ²⁹	n.g.	n.g.
Rössle 2000 ⁵⁸	<5	<3
Gines 2002 ⁸⁶	<10	<3
Sanyal 2003 ⁵²	<5	<1.5
Salerno 2004 ⁸⁷	<6	<3

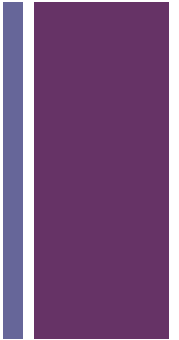
--Large variance in survival between the studies

--Study number 1: only 77% TIPS success → outlier

--Variance in inclusion criteria (TB, Cr, and recidivant/refractory ascites)



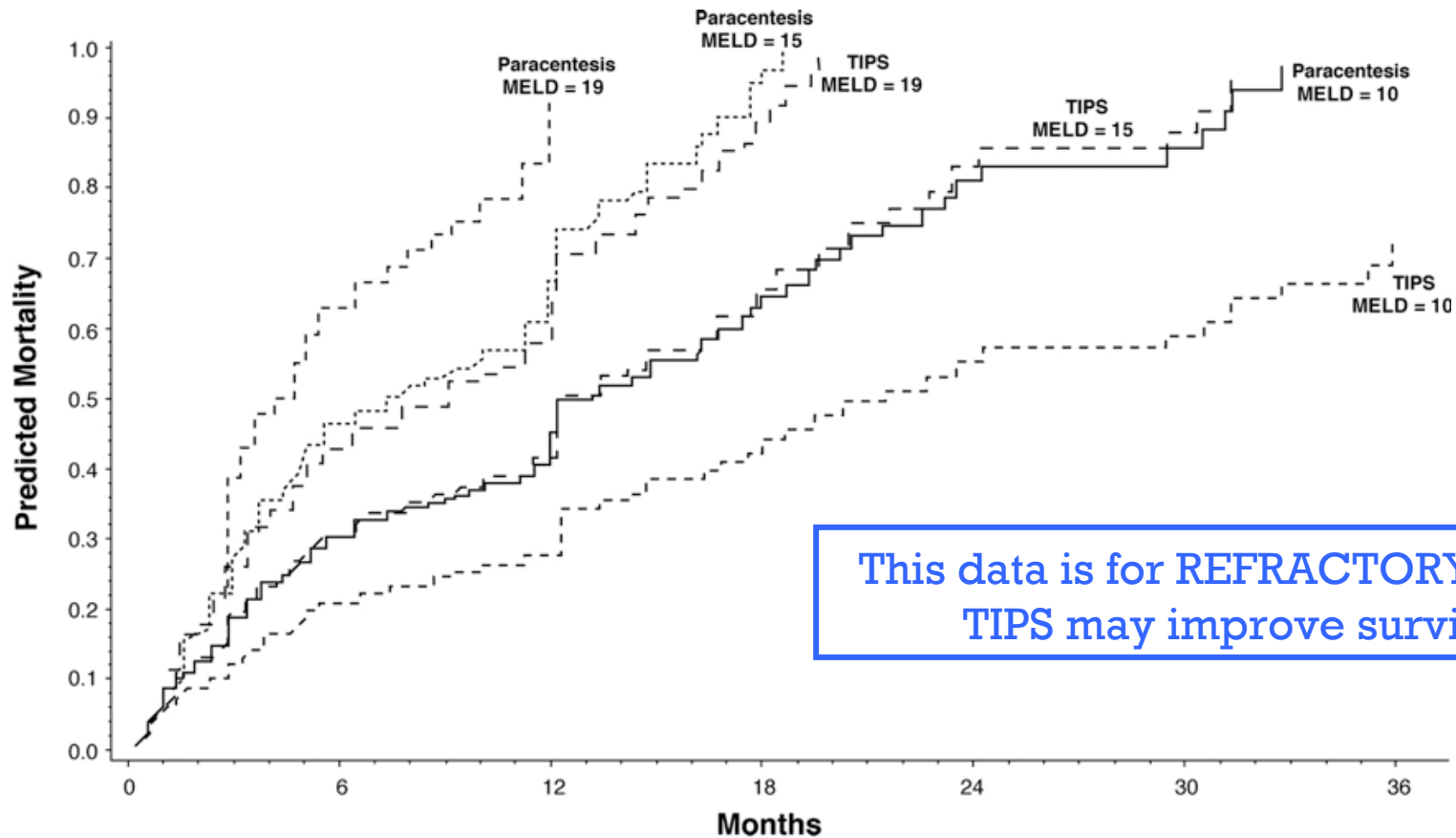
Does TIPS,
when performed for ascites,
affect survival?



- The meta-analysis we just looked at said NO.
- Let's look at more recent data:



Predicted mortality for TIPS /LVP based on MELD

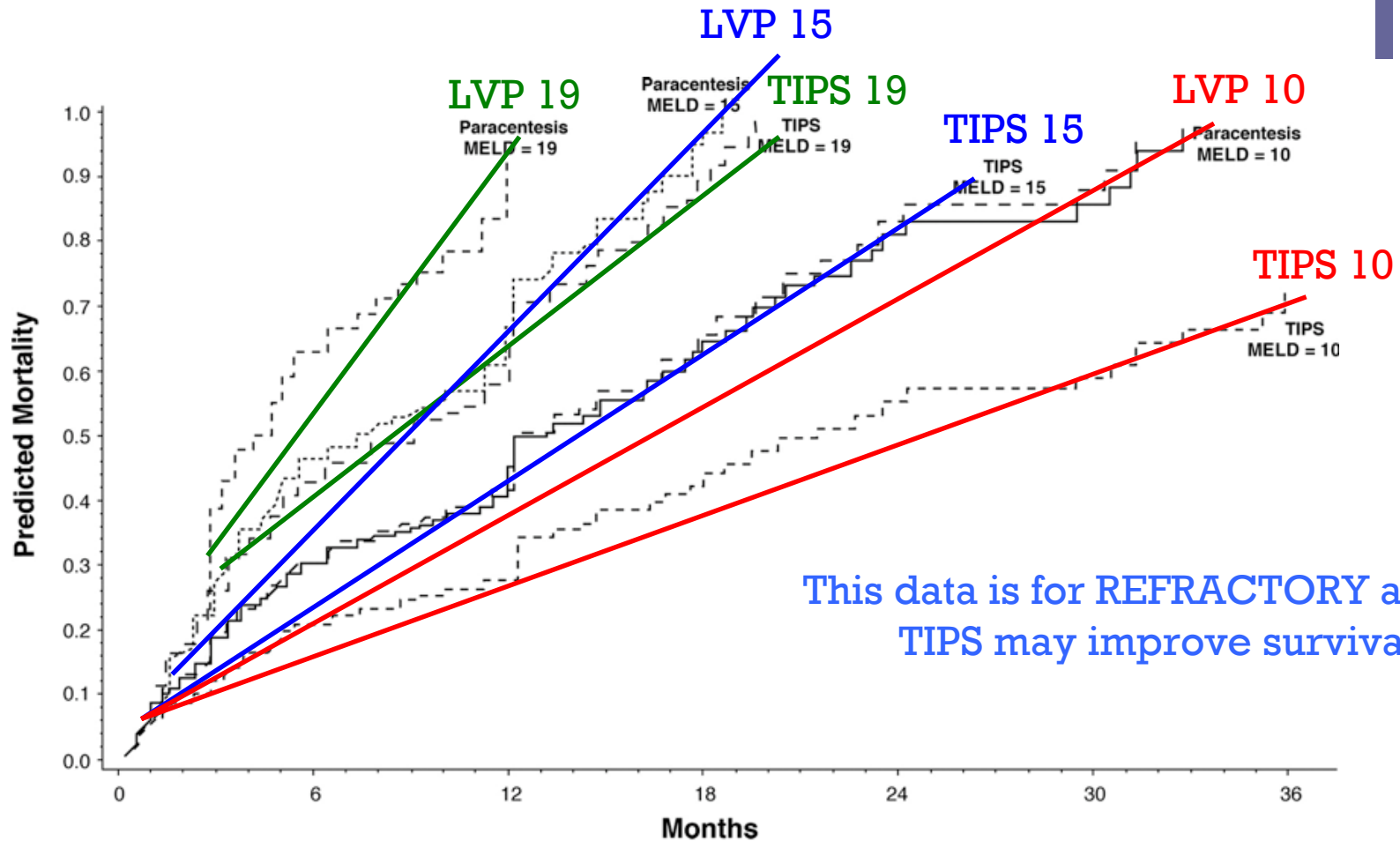


This data is for REFRACTORY ascites,
TIPS may improve survival.

[Salerno Gastroenterology 2007]



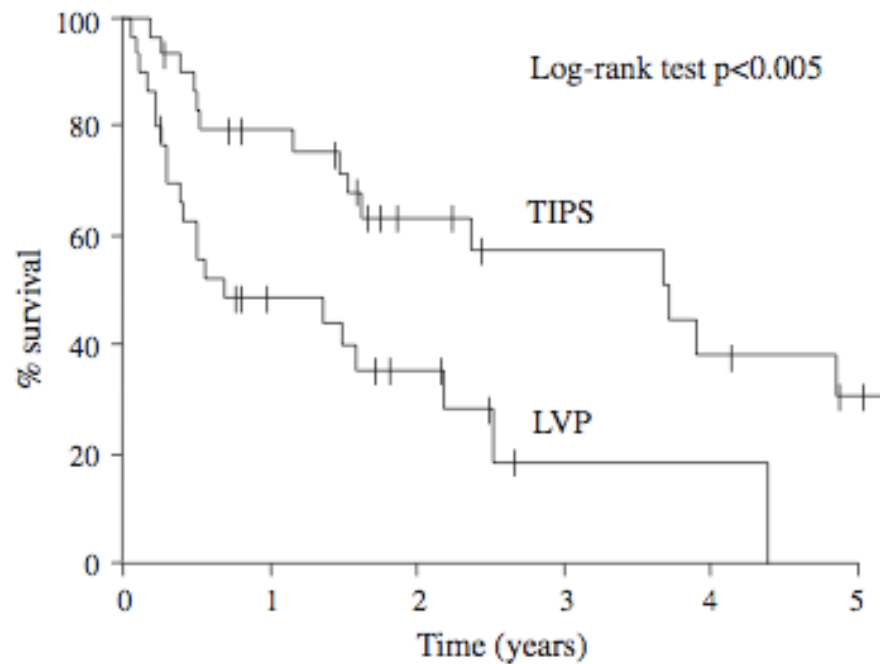
Predicted mortality for TIPS /LVP based on MELD



[Salerno Gastroenterology 2007]

+

TIPS vs. LVP ~ REFRACTORY ascites ~ Good Hepatic and Renal Function.

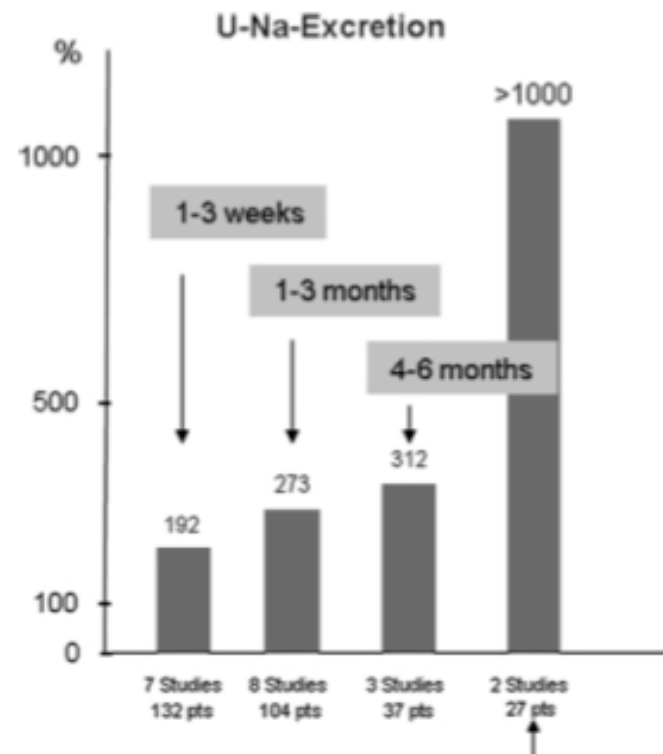
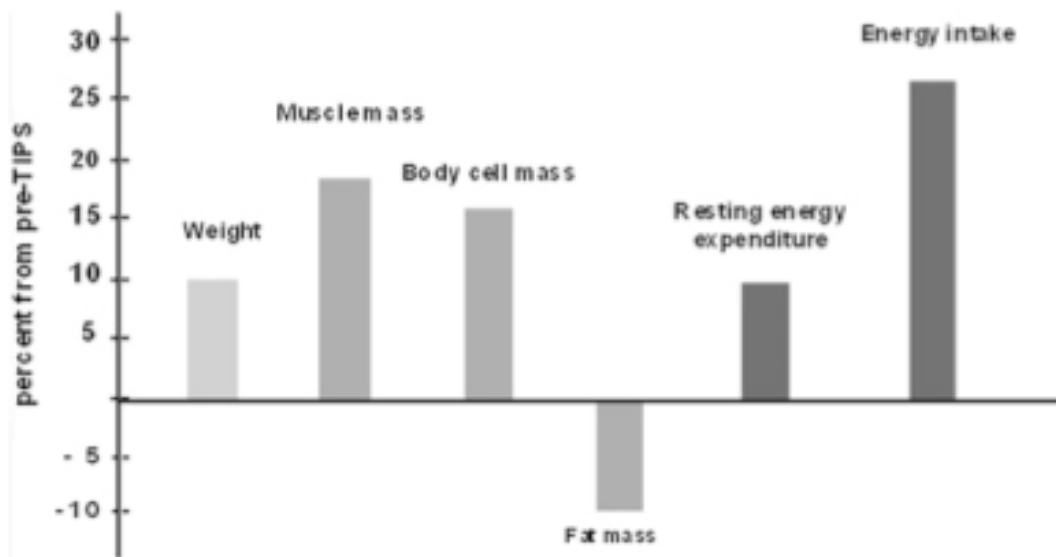


Patients at risk

TIPS	30	21	12	9	6	3
LVP	30	11	6	1	1	0

MELD ~9.6 in TIPS arm, ~10.6 in LVP arm

+ Post-TIPS Data



TIPS:

- improved urinary Na secretion and GFR
- improvement in serum Na
- decrease in renin and aldosterone
- improved protein metabolism and nutrition

- increased HE

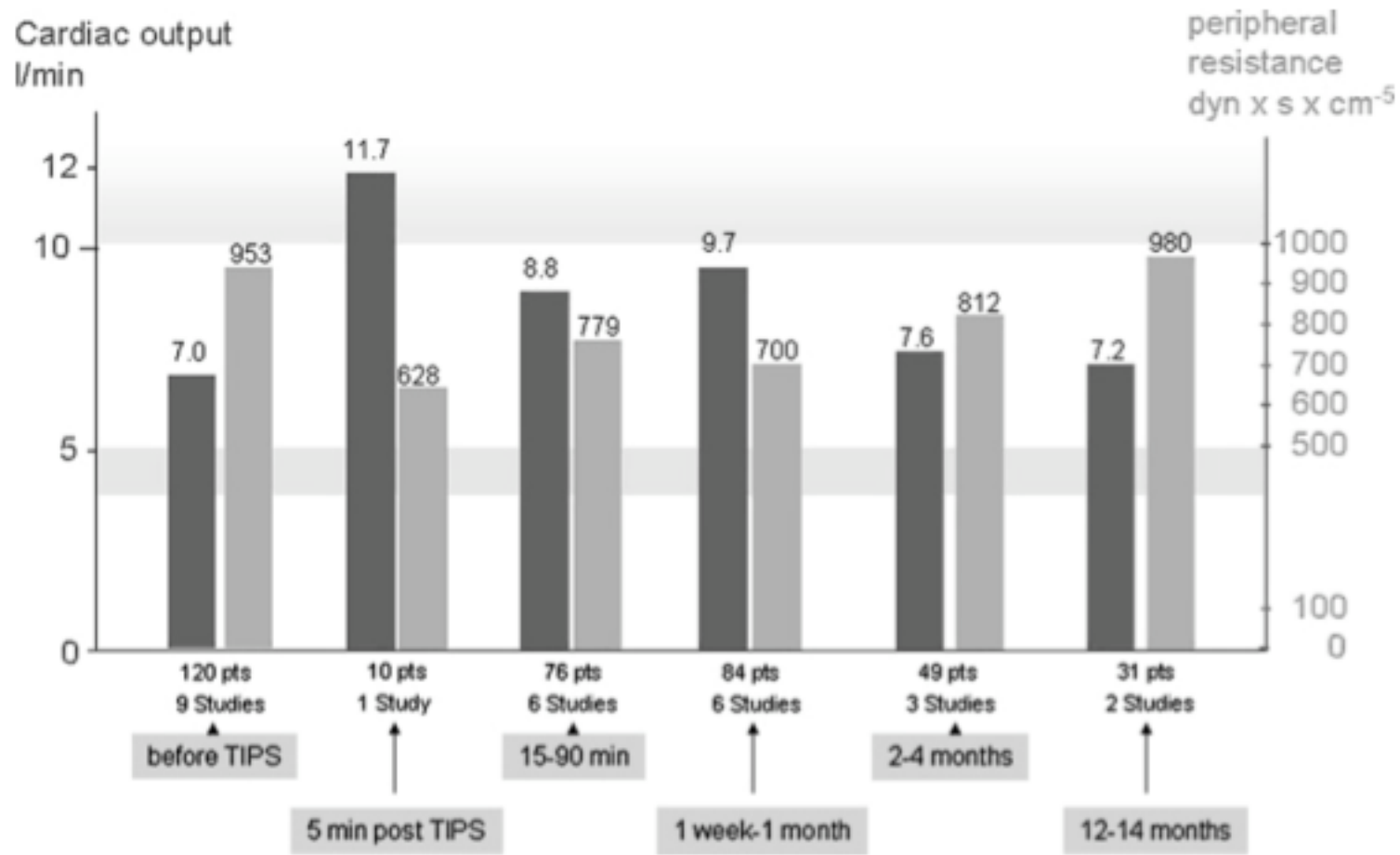
- increased liver deterioration if pre-TIPS

TP > 2

[Rossie Gut 2010]



+ Post-TIPS Hemodynamics



+ Pre-TIPS MELD + 3-month Mortality

MELD	A	B	Hosp w/o TIPS
10	15	27	1.6
12	17	30	2.2
14	22	37	3
15	23	39	3.5
16	25	42	4
17	28	46	5
18	30	49	6
19	32	52	7
20	35	57	8
21	38	60	9
22	43	64	11
23	43	71	12
24	47	73	14

***A =**
alcoholic/cholestatic

***B =**
viral/nash/mtx/wilson/
AIAT/crypto

***UNOS MELD**

Cr <1 = 1

Cr >4, HD = 4

TB < 1 = 1

INR < 1 = 1

+ The Bottom Line. . .

■ **TB > 3**

Independent predictor of 30-day mortality

■ **Each increase of 1 in the TB over 3** **40% increased risk of death**

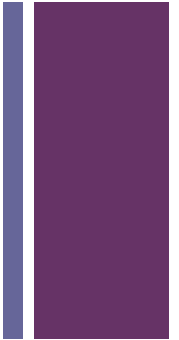
■ **AASLD GUIDELINES:**

- **Patients with high predicted 30-day mortalities (MELD > 15-18 or TB > 4) should be informed of their prognosis and TIPS performed only in the absence of other options.**



REMINDER:

**DON'T DO TIPS FOR PRIMARY
PROPHYLAXIS OF VB!**



- There are no trials on this
- Side effects of TIPS are well-established
- You will be triple-slapped!



TIPS for Secondary Prevention of VB

- First Line Treatment of Prevention of Variceal Bleeding
 - EVL and non-selective beta blockers
- Second-Line Treatment
 - TIPS likely better than endoscopic treatment for prevention of re-bleeding
 - TIPS does not translate to a survival advantage

Number of Patients	Rebleeding Rate		Encephalopathy		Mortality	
	Endo	PCS	Endo	PCS	Endo	PCS
376	49.8%	12.4%*	8.6%	17.2%**	28.8%	28.8%
811	46.6%	18.9%*	18.7%	34.0%**	26.5%	27.3%

--1990s data --Uncovered stents



Secondary Prevention of Variceal Rebleeding

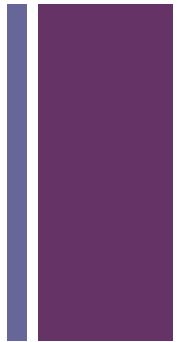


Table 1. Randomized Controlled Trials for the Use of TIPS vs Endoscopic Therapy as Secondary Prophylaxis of Variceal Hemorrhage

Study	Endoscopic therapy	n	Variceal rebleeding, %			Hepatic encephalopathy, %			Mortality, %		
			TIPS	ET	<i>P</i> value	TIPS	ET	<i>P</i> value	TIPS	ET	<i>P</i> value
Cabrera, 1996 ⁸⁶	ES	63	23	52	<.02	33	13	<.05	20	16	NS
Cello, 1997 ⁸⁷	ES	49	13	48	.012	58	44	.2	42	36	NS
Jalan, 1997 ⁸⁸	EVL	58	10	52	.0006	36	33	NS	42	20	NS
Sanyal, 1997 ⁸⁹	ES	80	22	21	NS	29	13	.001	29	18	.03
Sauer, 1997 ⁹⁰	ES or EVL	83	23	57	.0001	29	13	.041	29	27	NS
Rossle, 1997 ⁹¹	ES	46	15	41	<.001	36	18	.011	13	12	NS
Merli, 1998 ⁹²	ES	81	24	51	<.05	55	26	.006	24	19	.50
Garcia-Villareal, 1999 ⁹³	ES	46	9	50	.001	23	25	NS	15	33	<.05
Pomier-Layrargues, 2001 ⁹⁴	EVL	80	18	66	<.001	47	44	NS	41	41	NS
Sauer, 2002 ⁹⁵	EVL	85	19	30	NS	41	21	.041	19	17	NS
Gulberg, 2002 ⁹⁶	EVL	54	33	37	NS	8 ^a	4 ^a	—	20	17	NS
Garcia-Pagan, 2010 ³⁸	EVL	63	3	45	.001	25	39	NS	13	38	<.01

ES, sclerotherapy; ET, endoscopic therapy; NS, not statistically significant, *P* value not stated.

^aAt 1 month.

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.,

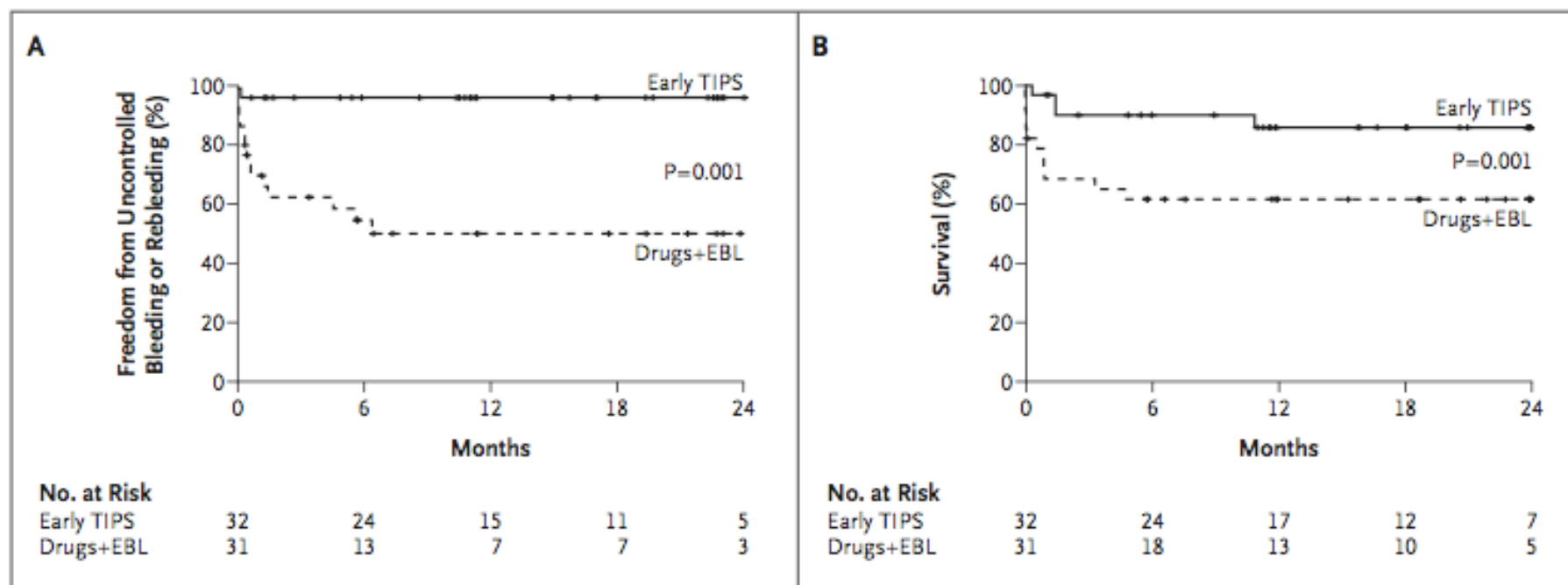


Figure 2. Actuarial Probability of the Primary Composite End Point and of Survival, According to Treatment Group.

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.

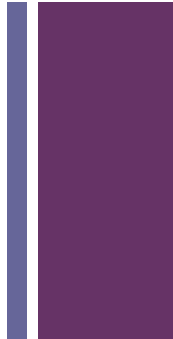


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Characteristic	Pharmacotherapy–EBL Group (N=31)	Early-TIPS Group (N=32)	P Value
Child–Pugh classification (no. of patients) [†]			0.99
Class B	16	16	
Class C	15	16	
Child–Pugh score	9.5±1.8	9.3±1.8	0.66
MELD score [‡]	16.9±6.3	15.5±5	0.28
MELD–Na score [§]	19±7	17±6	0.25
Ascites (no. of patients)	18	19	0.99
Bilirubin (mg/dl)	4.4±4.9	3.7±4.8	0.34
Albumin (g/liter)	26±7	26±7	0.89
Prothrombin time (%) [¶]	50±15	53±15	0.33
Creatinine (mg/dl)	1±0.4	1±0.5	0.59
Previous hepatic encephalopathy (no. of patients)	0	6	0.03

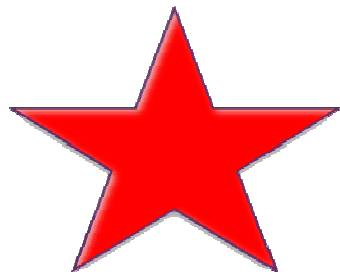


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Characteristic	Pharmacotherapy–EBL Group (N=31)	Early-TIPS Group (N=32)	P Value
Previous variceal bleeding in the absence of combined treatment (no. of patients)	5	11	0.15
Active bleeding at endoscopy (no. of patients)	22	23	0.99
Endoscopic treatment at time of index bleeding (no. of patients)			0.17
Band ligation	26	21	
Injection sclerotherapy	5	11	



Child C: only 10-13

Child B: were included if they had ACTIVE bleeding

Propanolol mean 55mg/day, ISMN added in 13

Exclusions: Cr > 3, age > 70

+ Risk Stratification for TIPS and 1-year Survival

LOW 80-90%	MEDIUM 50-80%	HIGH <50%
Elective prev of variceal rebleed	Elective for refractory ascites	Emergent for bleeding varices
MELD < 10	MELD 11-18	MELD > 18
CP A/B+	CP B-	CP C
Cr < 1.2		Cr > 1.7
TB < 2	TB 3-4	TB > 4
Normal Na	Na 130-140	Na < 130

+ Assessing Patency of TIPS

■ U/S with Doppler

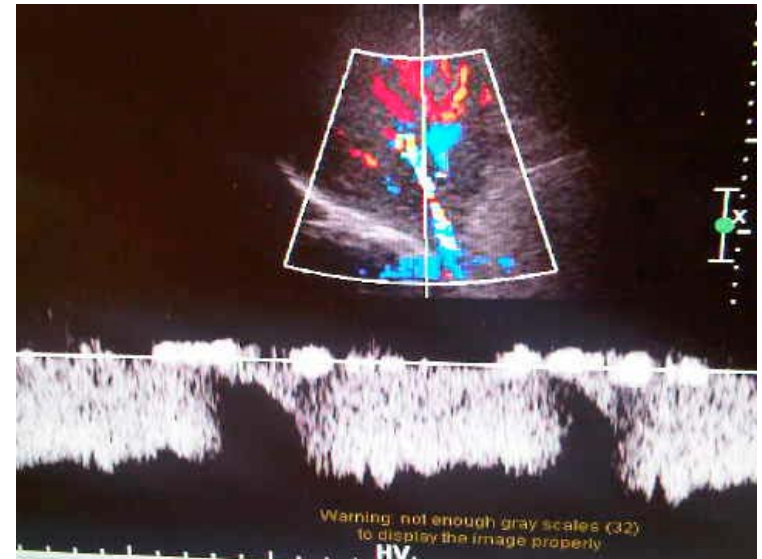
- Sensitivity for stenosis: ~ 10-35%
- Specificity for stenosis: ~ 90%
- Features: flow reversal, jet lesion, decreased flow

■ Best indicator of dysfunction

- Recurrence of indication for which TIPS was performed.
- Many pts will require continuation of diuretics after TIPS – this doesn't equate to TIPS dysfunction.

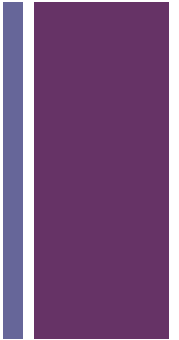
■ Angiography – gold standard

ABNORMAL U/S:
Predictive of TIPS malfunction.
NORMAL U/S:
Does not rule it out!



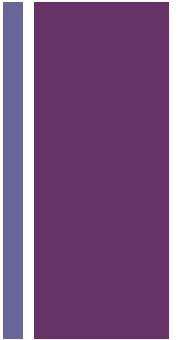


TIPS and Liver Transplantation



- All patients with TIPS should be considered possible transplant candidates.
- Stent should extend the least amount possible in the main PV and IVC to limit complications with transplant surgery.
- Be especially careful if pt is being considered for LDLT.
 - These pts need a cuff of hepatic vein.

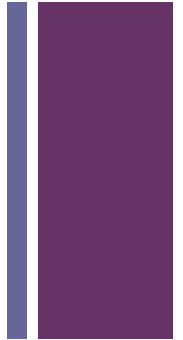
+ Review



- Anatomy and Portal HTN
- The Procedure
- Complications
- Indications (and Contraindications)



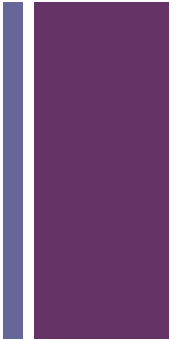
References/ Suggested Fellow Reading



- AASLD Guidelines: The Role of TIPS in the Management of Portal HTN.
- “Early Use of TIPS in Patients with Cirrhosis and Variceal Bleeding.” Garcia-Pagan et al. NEJM 362; 25: 2370-2379.
- “TIPS for treatment of refractory ascites, hepatorenal syndrome, and hepatic hydrothorax.” Rossle and Gerbes. Gut 2010; 59: 988-1000.
- “Using Transjugular Intrahepatic Portosystemic Shunts for Complications of Cirrhosis.” Bhogal and Sanyal. Clinical Gastroenterology and Hepatology 2011; 9: 936-946.



Meta-Analyses



- “A Meta-analysis of transjugular intrahepatic portosystemic shunt versus paracentesis for refractory ascites.” Albillos, Banares, et al. *Journal of Hepatology* 43 (2005) 990-996.
- “Transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis of individual patient data.” Salerno, Camma, et al. *Gastroenterology* 2007 Sept; 133(3): 825-34.