

TIPS

Focal Liver Lesions

Michael Krease, PGY IV

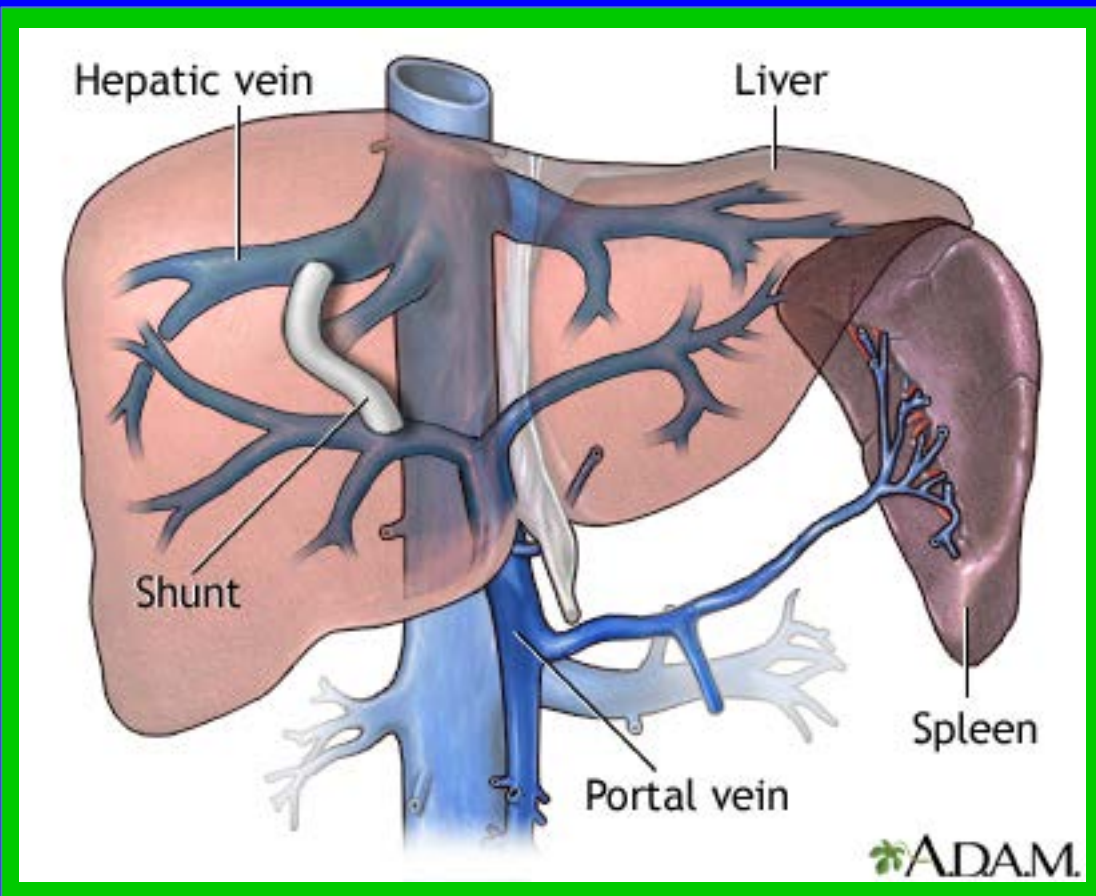


TIPS – Brief History

- **Has been in use for over 20 years**
- **Initially lack of consensus on appropriate patient selection**
- **1995 NIH Meeting – effective in acute control and prevention of recurrent bleeding from EV**
 - **Unclear as to usefulness in other complications of portal HTN**
- **Since then over 1,000 papers published and numerous clinical trials allow for more definitive recommendations**



TIPS – The Procedure

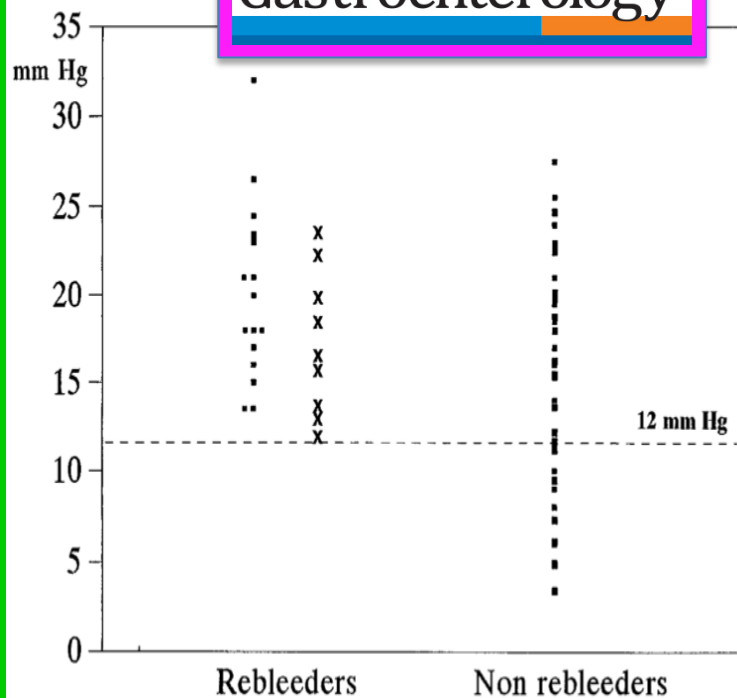


- **Decompress portal vein!!**
- **What gradient is best??**

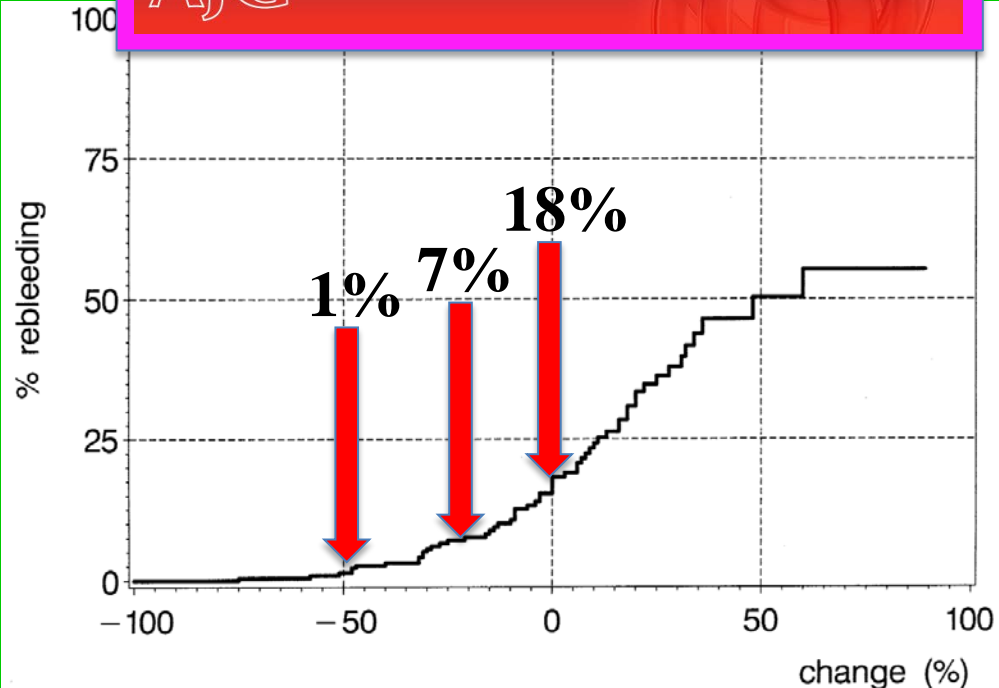
TIPS – Gradients

- Successful TIPS defined as reduction of HVPG to less than 12mmHg
- Esophageal varices – gold standard for prevention of rebleeding remains HVPG < 12 mm Hg¹
 - Recent data suggests HVPG < 12 mm Hg may not be needed²

Gastroenterology



AJG The American Journal of GASTROENTEROLOGY



1 - Casado M, Bosch J, Garcia-Pagan JC, Bro C, Banaras R, Rondi JC, Escorsell A, et al. Clinical events after transjugular intrahepatic portosystemic shunt: correlation with hemodynamic findings. *Gastroenterology* 1998;114:1296-1303.

2 - Rosale M et al. How much reduction in portal pressure is necessary to prevent variceal rebleeding? A longitudinal study in 225 patients with transjugular intra-hepatic portosystemic shunts. *Am J Gastroenterol* 2001;96:3379-3383

TIPS – Gradients

- Ascites - optimal gradient for control of refractory ascites less clear...
 - Previously shown ascites does not occur when HVPG < 8mmHg
 - Development of ascites reflection of renal and hepatic function
- Gastric varices
 - Gradient to prevent rebleeding may be < than 12 mm Hg
 - surveillance

GASTROENTEROLOGY 2003;124:634–641

CLINICAL—LIVER, PANCREAS, AND BILIARY TRACT

The North American Study for the Treatment of Refractory Ascites

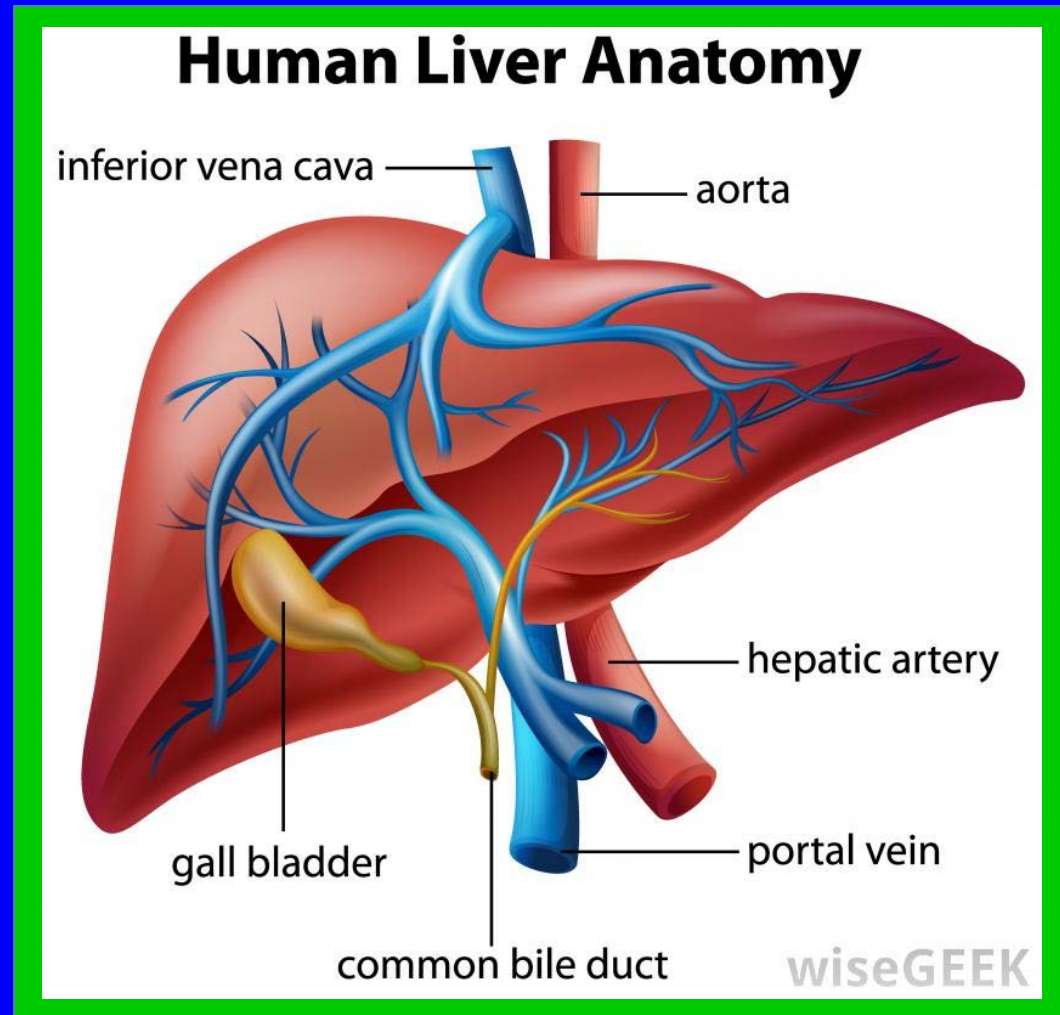
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Gastroenterology

TIPS – Gradients

- Measurement not standardized
- Classically, free and wedged hepatic vein P measured, difference between them is HVPG
- Post-TIPS RA vs. IVC



TIPS – Pre TIPS evaluation

- Labs – CBC, CMP, PT/INR
- Cross sectional imaging by CT or MRI
- If history of CHF, TR, pulmonary HTN then 2D ECHO
 - In absence of cardiac history 2D ECHO not necessary
 - Others believe it should be performed on all patients

Table 2. Contraindications to Placement of a TIPS

Absolute

Primary prevention of variceal bleeding
Congestive heart failure
Multiple hepatic cysts
Uncontrolled systemic infection or sepsis
Unrelieved biliary obstruction
Severe pulmonary hypertension

Relative

Hepatoma especially if central
Obstruction of all hepatic veins
Portal vein thrombosis
Severe coagulopathy (INR > 5)
Thrombocytopenia of < 20,000/cm³
Moderate pulmonary hypertension

TIPS – Outcome

- **Models to predict outcome**
 - **MELD – accurate for 3 month and 1 year survival**
 - **Second model – 3 month survival**
 - **Bilirubin > 3 (1 point)**
 - **ALT > 100 (1 point)**
 - **Pre-TIPS encephalopathy (1 point)**
 - **Urgency of TIPS (2 points)**
 - **Short term survival predicted by bilirubin alone**
 - **Bilirubin > 4 – increased 30 day mortality**
- **0 – low risk**
 - **1-3 – medium risk**
 - **4-5 – high risk**

TIPS – Complications

- **TIPS dysfunction – loss of portal decompression due to occlusion or stenosis of the TIPS**
 - **50% stenosis**
 - **Rise in HVPG to > 12 mm Hg**
 - **Recurrence of complication for which it was placed**

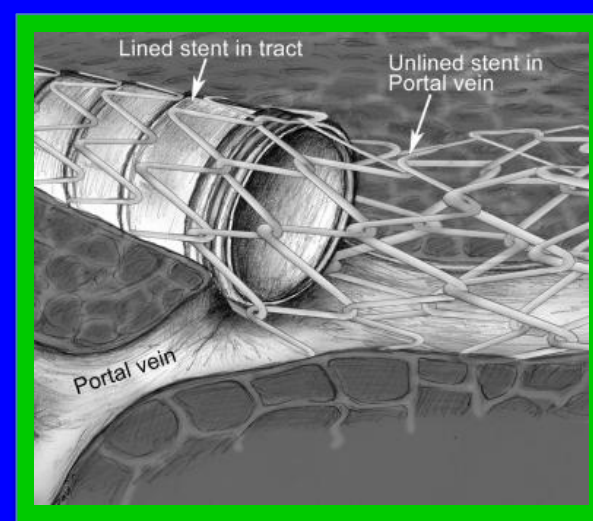


TIPS – Complications

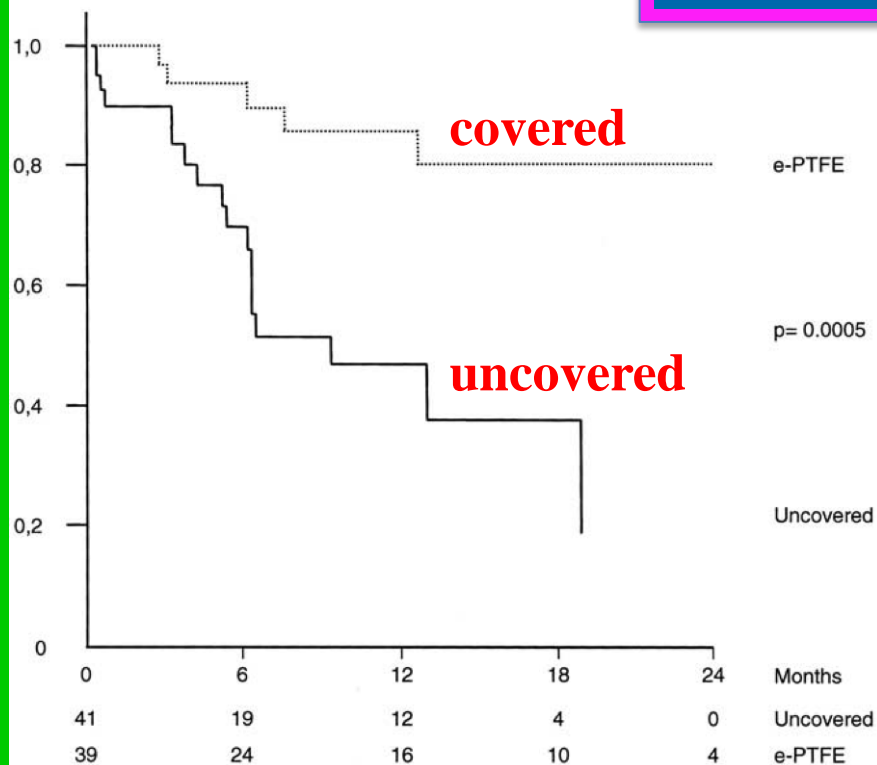
- **TIPS occlusion**
 - **thrombosis vs. intimal hyperplasia**
 - ↓
 - **Can occur within 24 hours**
 - **Cause: leakage of bile, hypercoaguable disorder, insufficient stent coverage**
 - **Identified by doppler US**
 - ↓
 - **Collagenous matrix covered by endothelial cells**
 - **Incidence varies depending on surveillance technique used**
- **Puncture of liver capsule → intraperitoneal bleeding (1-2%)**
- **Hemolysis**
- **Hepatic encephalopathy**

TIPS – type of stent

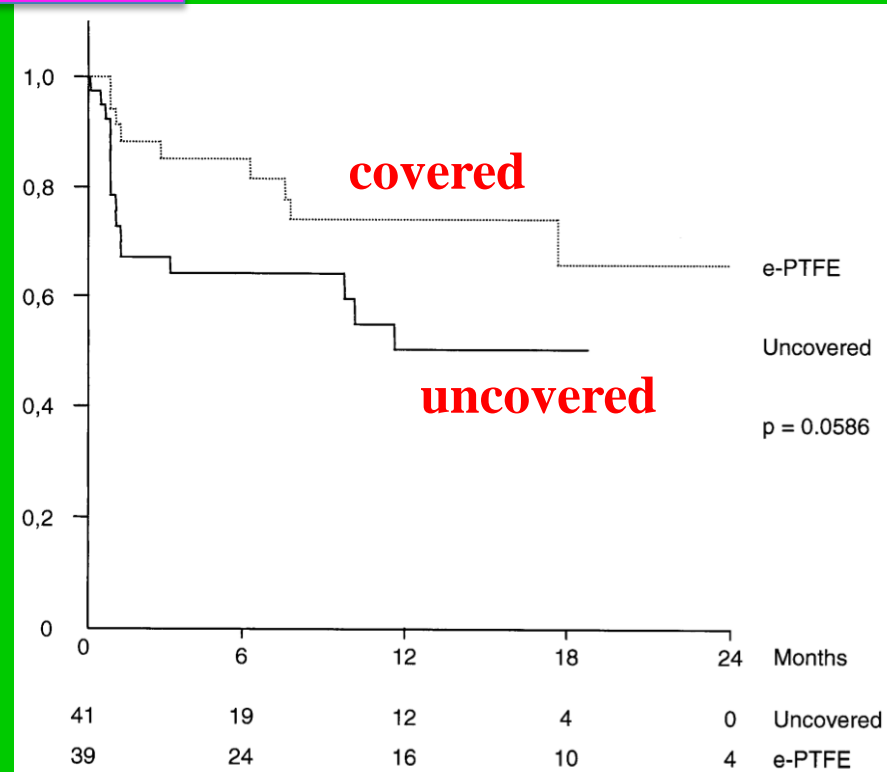
- 2004 – designed to study patency rates between bare stent compared to PTFE covered stents



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Probability of remaining free of shunt dysfunction



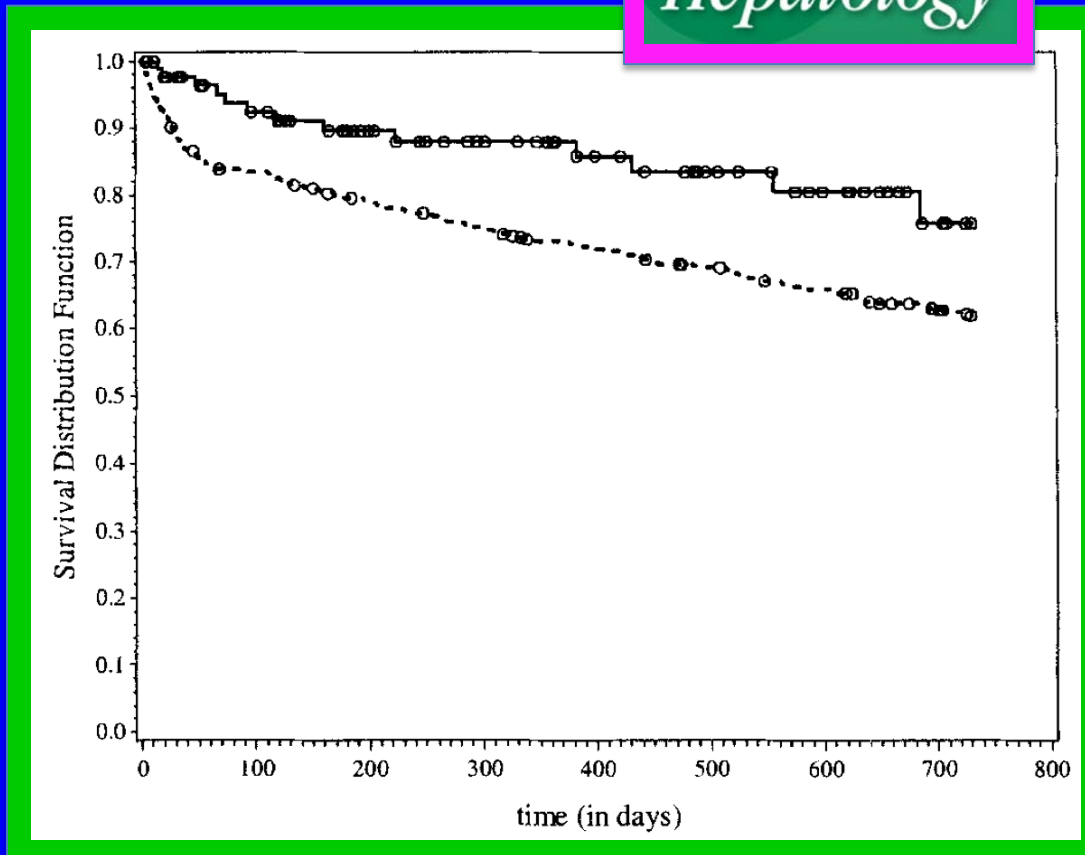
Probability of remaining free of encephalopathy

TIPS – type of stent



- 2003 retrospective study from Austria
- Elective TIPS for prevention of variceal rebleeding, refractory ascites
- Emergent cases excluded

Hepatology

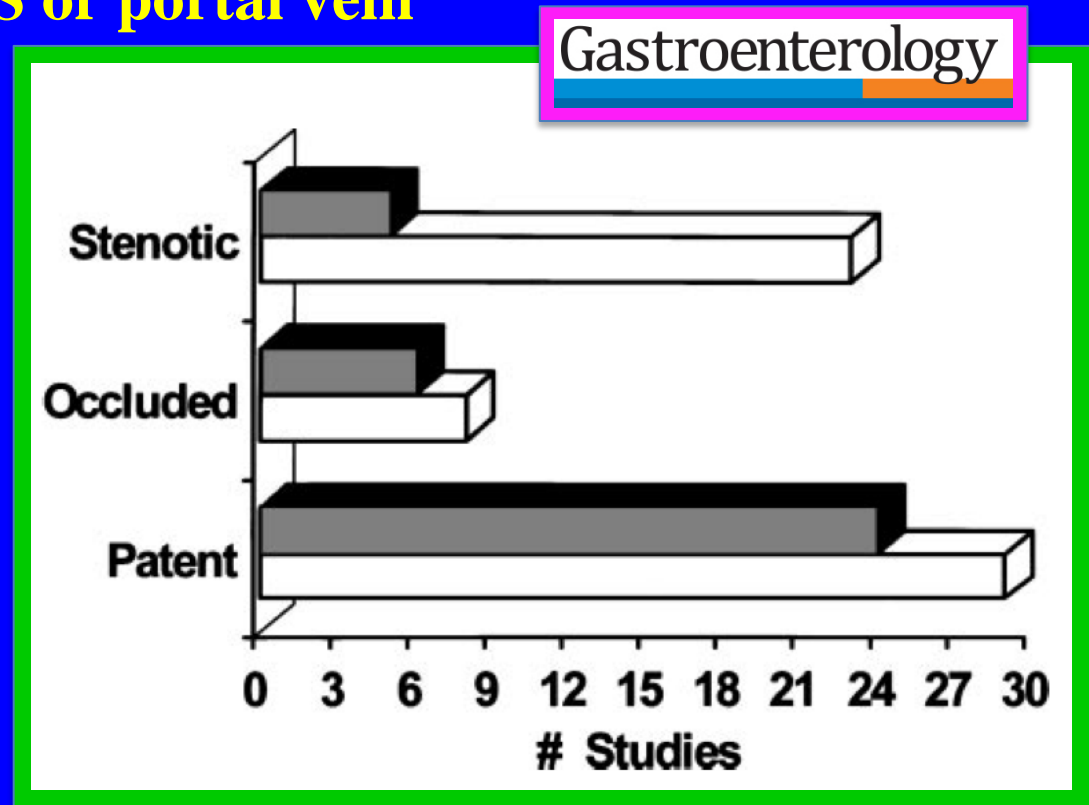


TIPS – Complications

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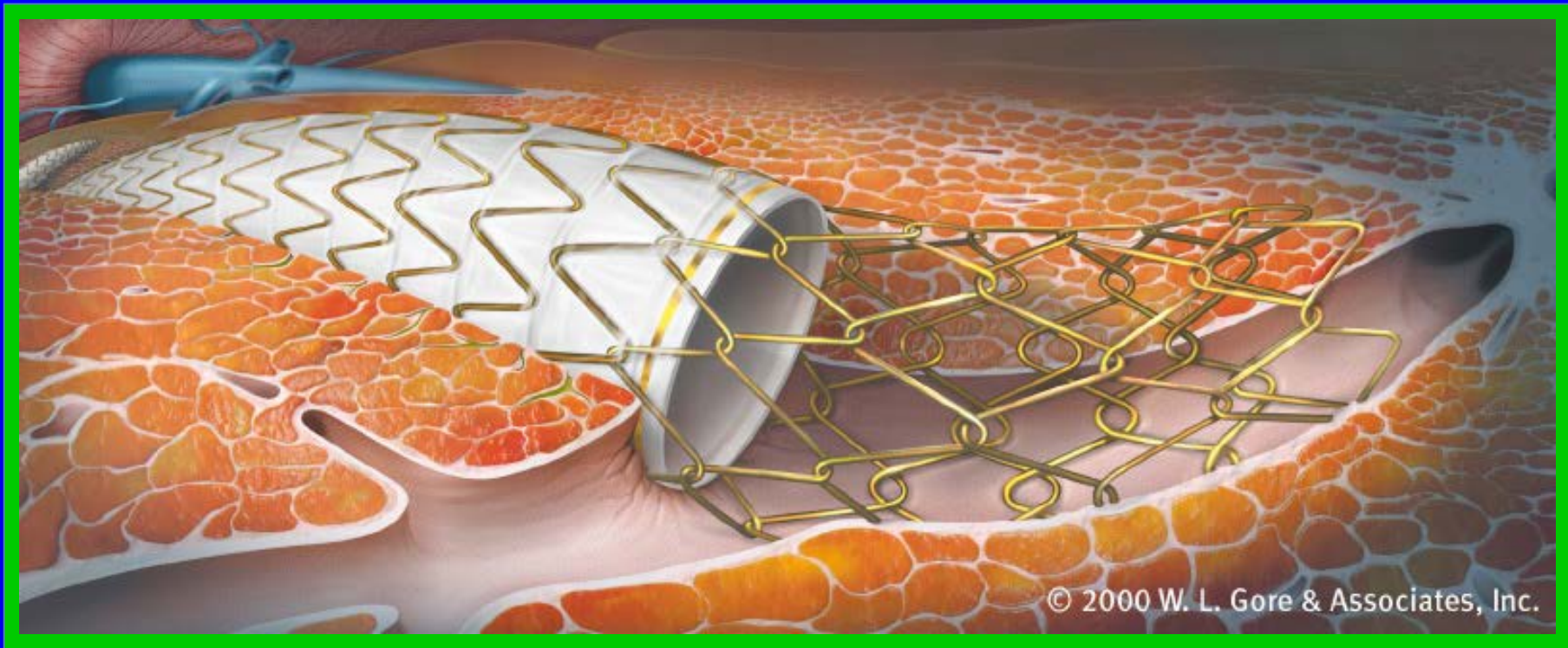
TIPS – surveillance

- Most physicians rely on Doppler US to identify TIPS stenosis
- US features used to identify TIPS stenosis:
 - Flow reversal
 - Jet lesion
 - Decreased flow in TIPS or portal vein
- Sensitivity 35%
- Difficulty is that US is a modality which measures velocity, and diameter is estimated
- Abnormal US indicates dysfunction, normal does not exclude dysfunction
- Best indicator of TIPS dysfunction is recurrence of initial problem for which it was initially placed



TIPS – Complications

- Nearly all long-term survivors after TIPS experience TIPS stenosis within the first 2 years
- Commonly used regimen:
 - Angiography at 6 and 12 months, then annually thereafter for 3 years



TIPS – Complications

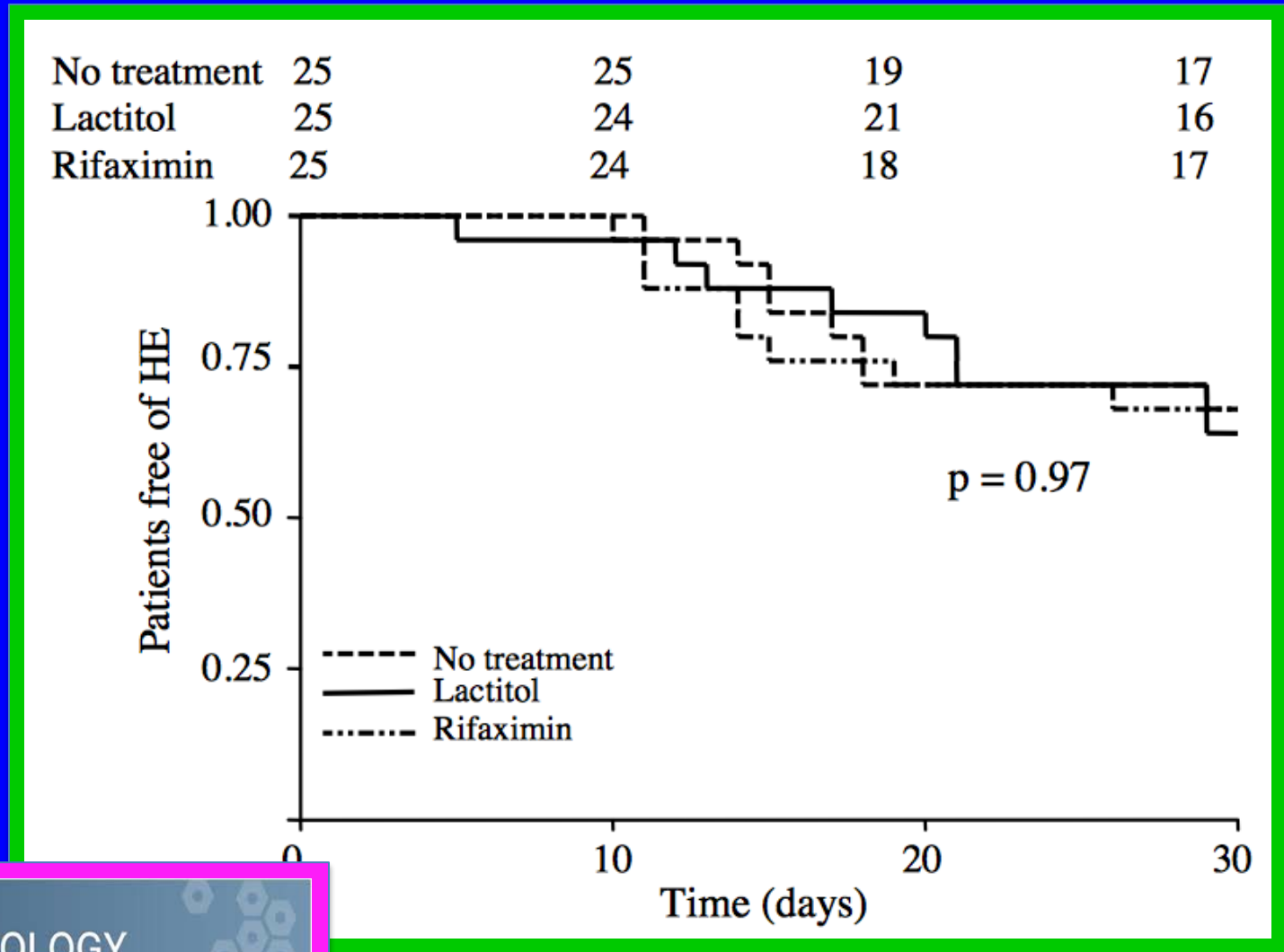
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- **Hepatic encephalopathy**

TIPS – Complications - HE

- Other than TIPS dysfunction, HE has limited effectiveness of TIPS most significantly
- Incidence of new or worsening HE 20-31%
- Only if refractory to medical management is TIPS contraindicated
- If HE secondary to bleeding, prevention of recurrent bleeding by TIPS will make it less likely patient experiences recurrent HE
- Prophylactic use of nonabsorbable disacharides or antibiotics in prevention of post-TIPS HE??



TIPS – Complications - HE



TIPS – Complications - HE

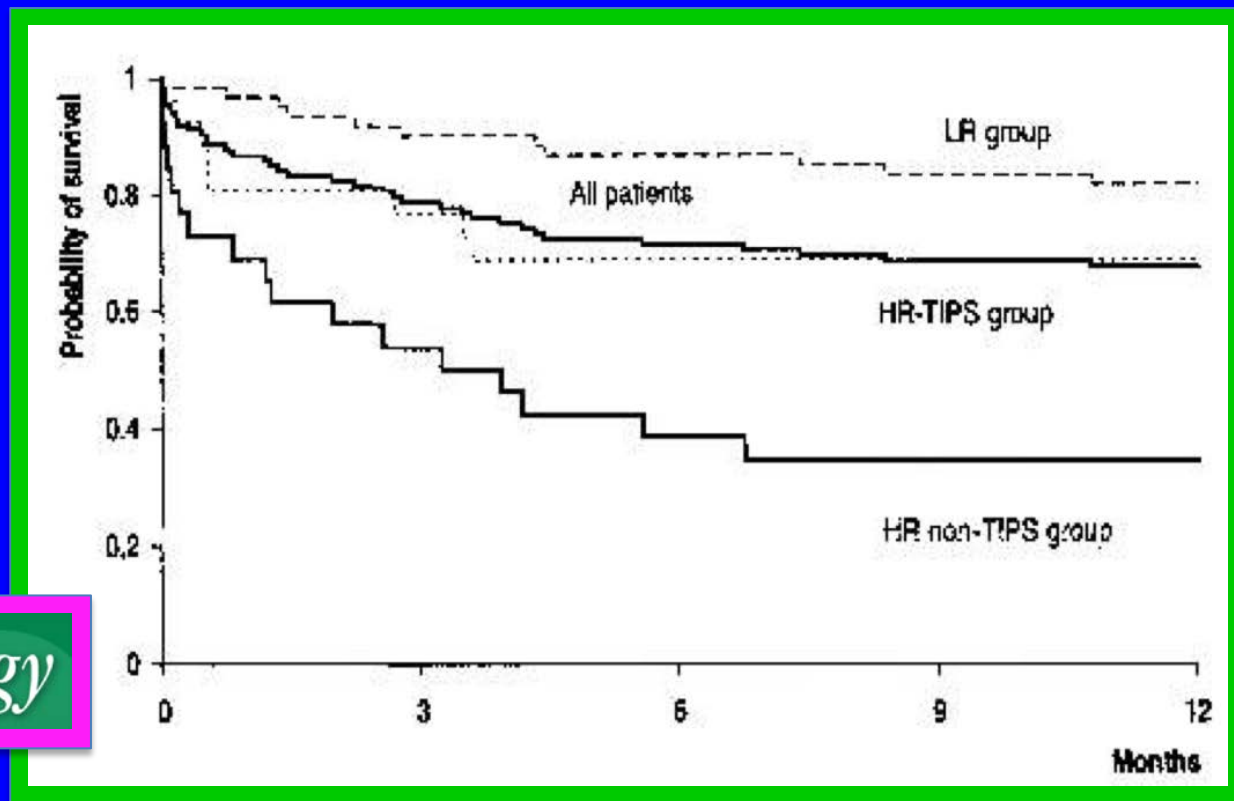
No treatment	25	25	19	17
Lactitol	25	24	21	16

Treatment	Basal	Two weeks	Four weeks
<i>Ammonia (mcg/dl)</i>			
No-treatment	65 ± 8.7	117.4 ± 12.8*	126.4 ± 17.8*
Lactitol	66 ± 11.3	112 ± 10.5*	122.4 ± 22.6*
Rifaximine	62.1 ± 9.1	110.8 ± 12.5*	125 ± 12.7*
<i>TMT-A Z-score</i>			
No-treatment	1.28 ± 0.2	1.1 ± 0.3	1.2 ± 0.3
Lactitol	1.72 ± 0.2	1.72 ± 0.3	1.17 ± 0.3
Rifaximine	1.41 ± 0.2	1.6 ± 0.2	1.31 ± 0.2

0 10 20 30
Time (days)

TIPS – Indications

- Primary prevention of variceal hemorrhage – NO!!
 - Increased mortality
- Acutely bleeding esophageal varices refractory to medical tx.
 - Urgency of TIPS an independent predictor of early mortality
 - 31-77% mortality has been reported



Hepatology

TIPS – Indications

- **Esophageal variceal rebleeding**
 - **Once EV have bled, risk of rebleeding is 50%**
 - **Surgical shunts compared to endoscopic therapy decreased rebleeding rates at expense of increased HE**
 - **It was hoped that TIPS would have same effect on rebleeding with decreased HE**
 - **1999 – meta-analysis of 11 published controlled trials**
 - **Less rebleeding compared to endoscopic therapy but with increased HE and no mortality benefit**

16. Pending the development of tests that accurately predict the risk of rebleeding, TIPS should not be used for the prevention of rebleeding in patients who have bled only once from esophageal varices. Its use should be limited to those who fail pharmacologic and endoscopic therapy. Evidence-I

TIPS – Indications

- June 2010 – early TIPS associated with reduction in mortality and no increase in HE
 - CTP B and C included (up to 13)
 - PTFE stents used



The NEW ENGLAND
JOURNAL of MEDICINE

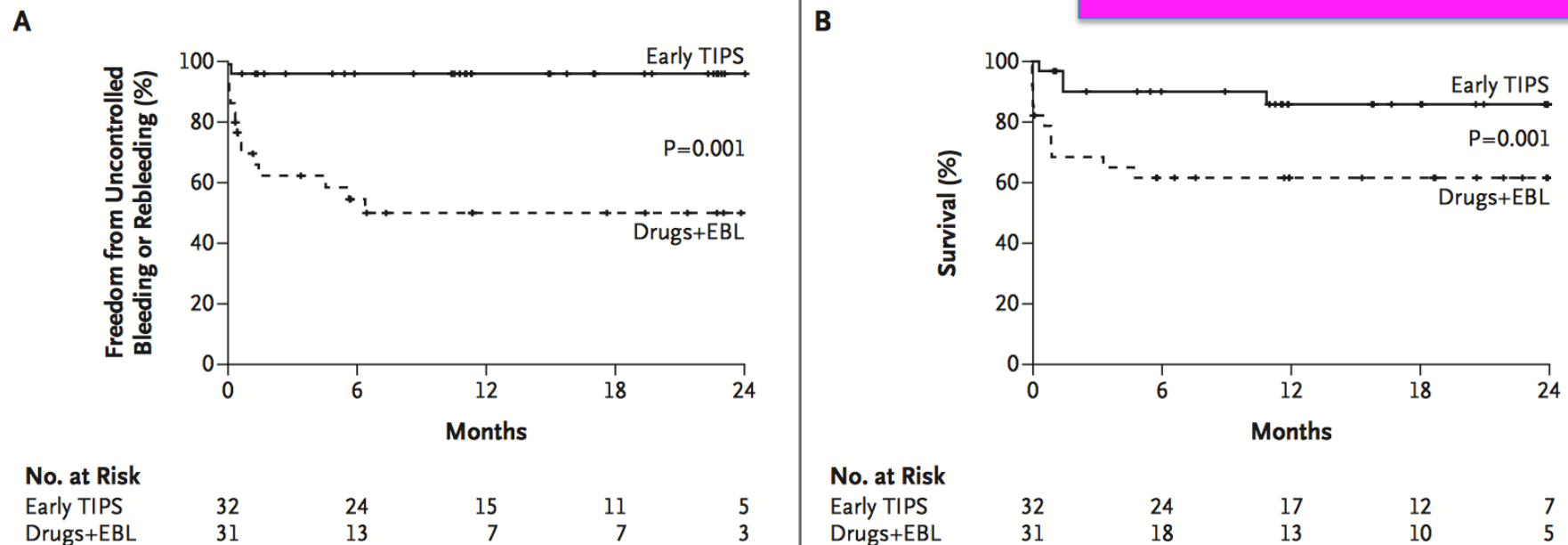


Figure 2. Actuarial Probability of the Primary Composite End Point and of Survival, According to Treatment Group.

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.

TIPS – Indications

- TIPS effective on control of bleeding gastric varices
 - HVPG required may be lower than for EV
 - Embolization of the gastric varices at time of TIPS may be required
- Use of TIPS in PHG should be limited to those who have recurrent bleeding despite use of beta-blockers
- TIPS not effective in controlling bleeding from GAVE



TIPS – Indications

- Refractory ascites – 50% mortality in 12 months
- TIPS??

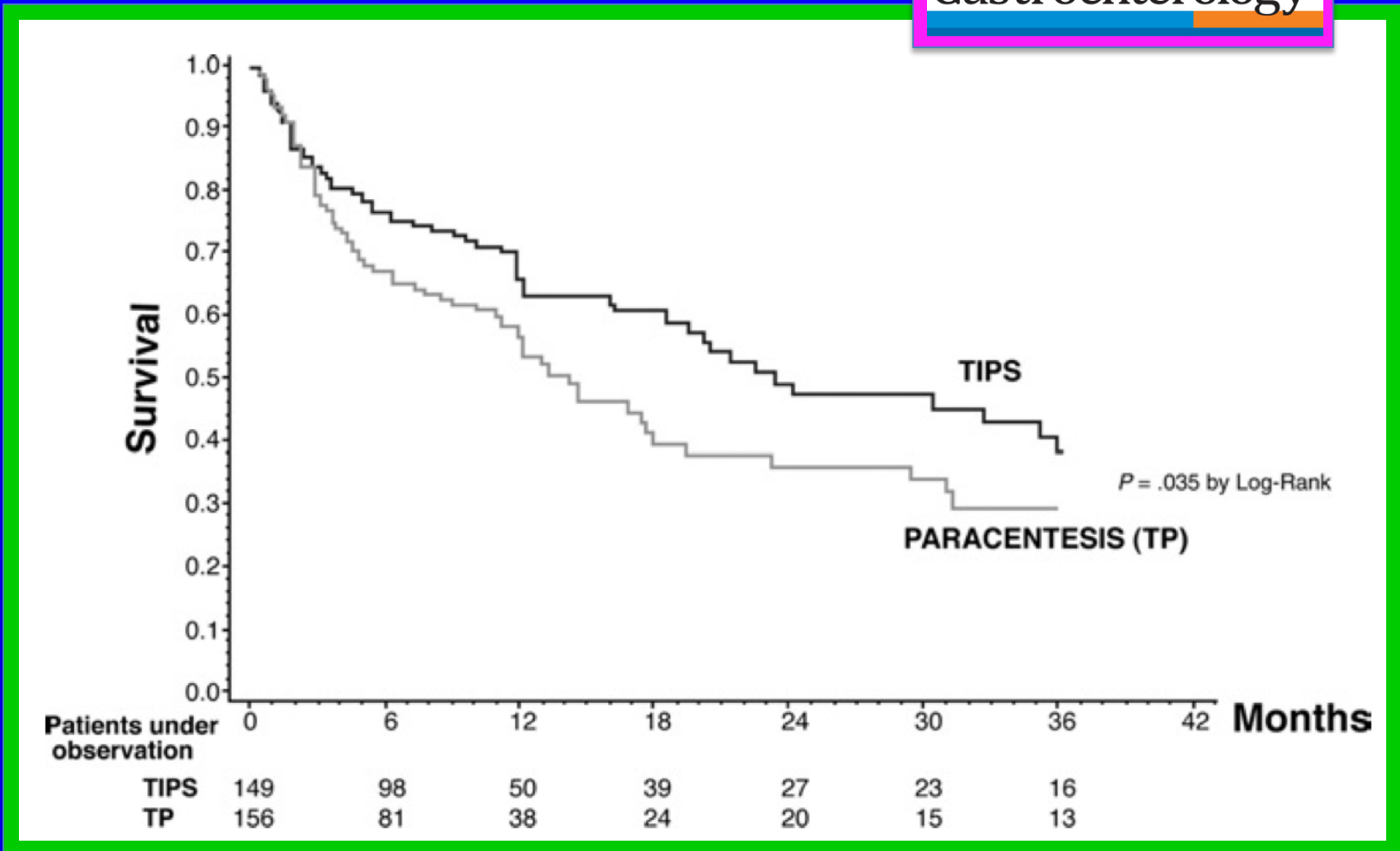
Table 6. TIPS Versus Large Volume Paracentesis in Treatment-Refractory Cirrhotic Ascites

Reference Number	Number of Patients		Ascites Improved		Survival@		New or Severe Encephalopathy	
	TIPS	LVP	TIPS	LVP	TIPS	LVP	TIPS	LVP
98	13	12	38%	0%	29%	60%	15%	6%
99	29	31	84%*	43%	58%	32%	23%	13%
100	35	35	51%*	17%	26%	30%	60%*	34%
23	52	57	58%*	16%	35%	33%	38%	21%
101	33	33	79%*#	42%	59%*	29%	61%	39%

TIPS – Indications

- Meta-analysis from 2007 showed improved mortality from TIPS for refractory ascites
- No increase in HE

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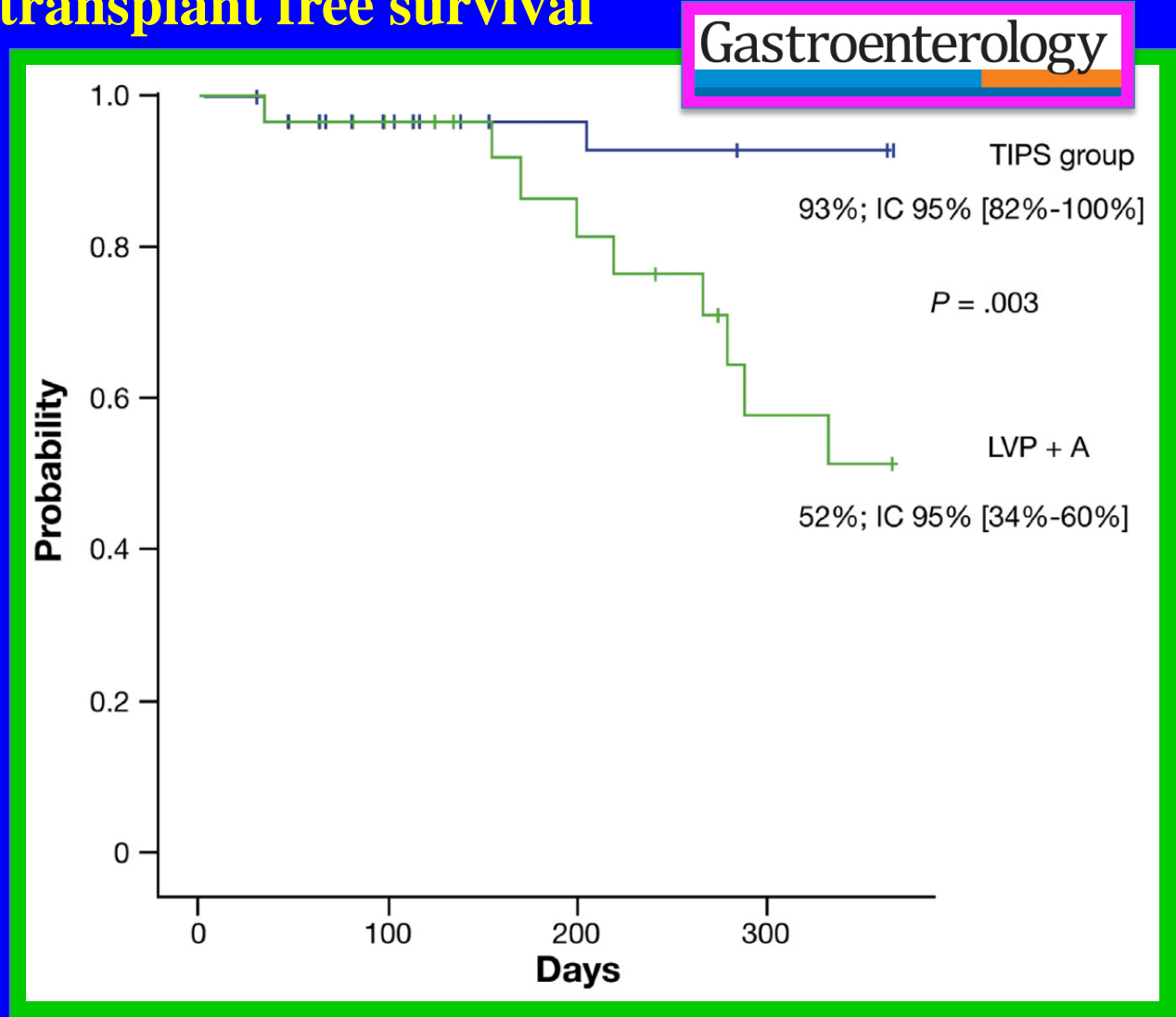
TIPS – Indications

- Substantial heterogeneity in terms of design, methods, and quality has led to the following recommendation:

22. TIPS will decrease the need for repeated large volume paracentesis in patients with refractory cirrhotic ascites. However, given the uncertainty as to the effect of TIPS creation on survival and the increased risk of encephalopathy, TIPS should be used in those patients who are intolerant of repeated large volume paracentesis. Evidence-I

TIPS – Indications

- 2017 – TIPS with PTFE covered stent vs. repeat LVP
 - TIPS increased transplant free survival
 - No difference in HE

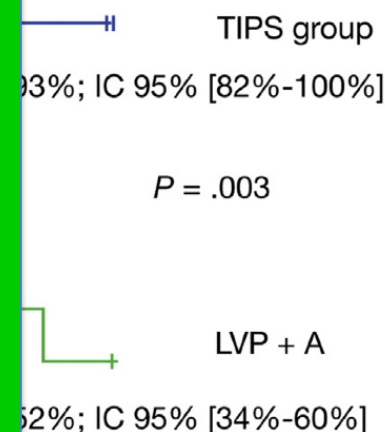


TIPS – Indications

- 2017 – TIPS with PTFE covered stent vs. repeat LVP

Outcome	TIPS (n = 29)	LVP+A (n = 33)
No. of paracenteses per patient, mean ± SD	1 ± 1	10 ± 7***
Volume extracted, L/patient, mean ± SD	6 ± 10	64 ± 47***
Albumin infusion, g/patient, mean ± SD	39 ± 70	550 ± 458***
Days in hospital, mean ± SD	17 ± 28	35 ± 40*
Patients with OHE, n	10	11
Episodes of OHE per patient, n, mean ± SD	1.6 ± 0.7	1.7 ± 0.8
Patients with OHE grade >2, n	4	7
Patients with PHT-related bleeding, n	0	6**
Patients with hernia-related complication, n	0	6**
Patients with HRS, n	0	1
Patients with SBP, n	0	2
Patients with sepsis, n	5	9
HCC, n	0	1

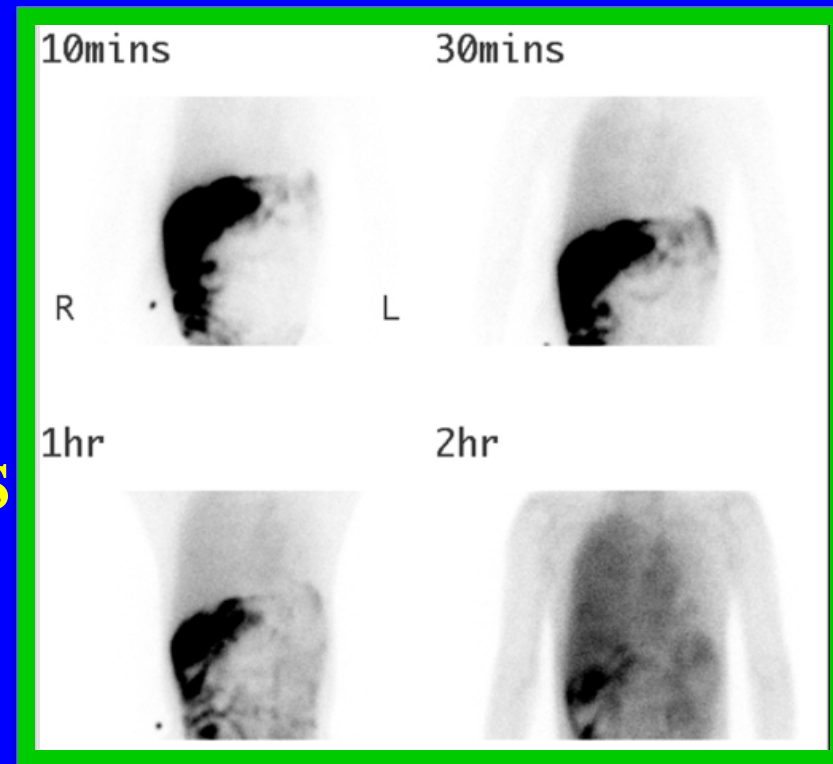
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Days

TIPS – Indications

- **Refractory hepatic hydrothorax (HH)**
 - TIPS effective in control of HH but should only be used in patients whose effusion can not be controlled by diuretics and Na restriction
- **Hepatorenal syndrome – no controlled trials have been done**
 - When TIPS was compared to LVP, reduced incidence of HRS in those who received TIPS was observed
 - Currently, no recommendation for the use of TIPS in HRS
- **Hepatopulmonary syndrome – TIPS not recommended**



FLL - Introduction

- Widespread use of imaging modalities as led to increased discovery of previously unsuspected liver lesions in otherwise asymptomatic patients
- Between 1996 and 2010:
 - CT tripled
 - MRI quadrupled
 - US doubled
 - PET increased by 57%
- Critical components once FLL identified:
 - H/P (OCP)
 - Radiology
 - Pathology



FLL – Specific lesions

BENIGN

- Hepatocellular adenoma
- Hemangioma
- Focal nodular hyperplasia (FNH)
- Nodular regenerative hyperplasia (NRH)
- Simple hepatic cysts
- Hydatid cysts

MALIGNANT

- Hepatocellular carcinoma (HCC)
- Cholangiocarcinoma (intrahepatic)



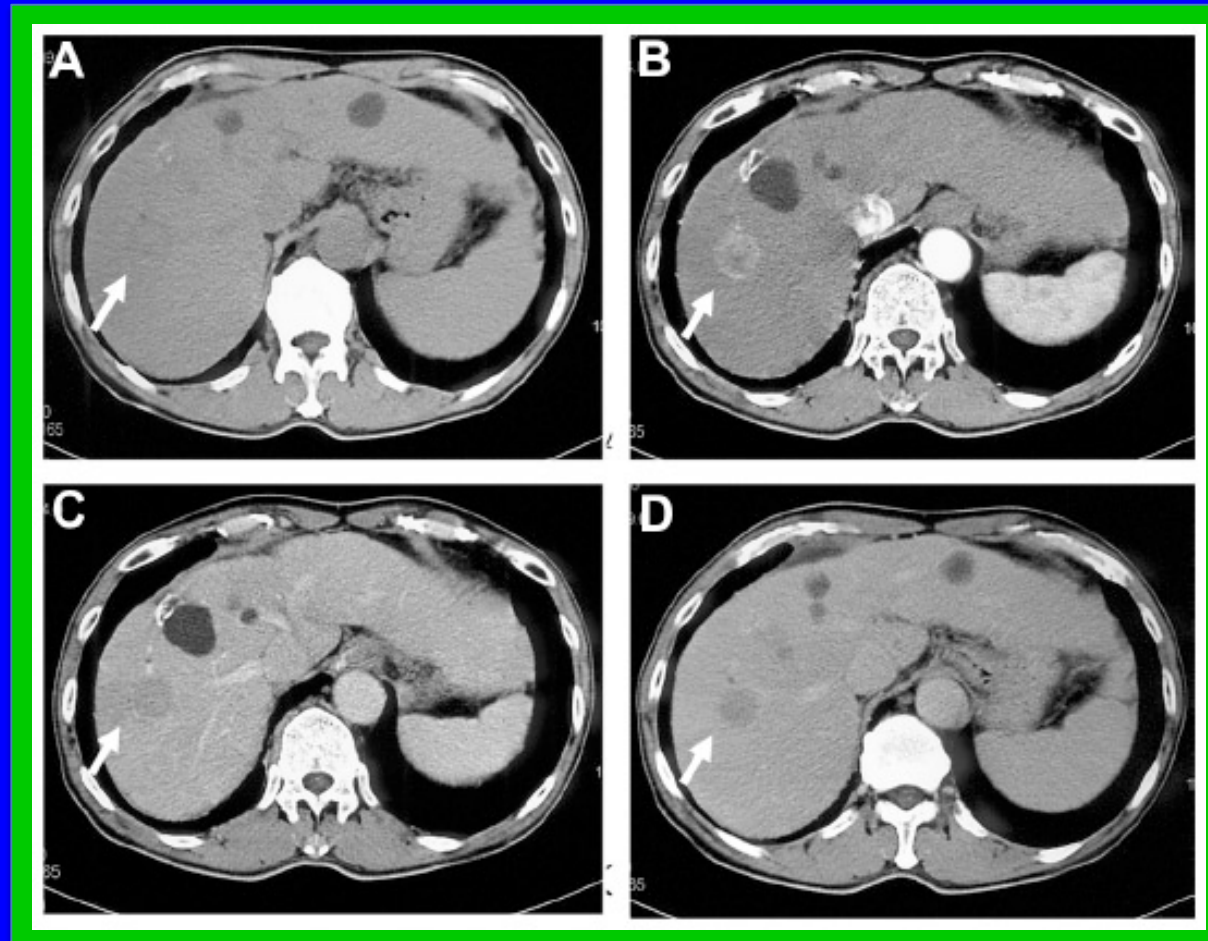
FLL – HCC

- 3rd most common tumor worldwide
- 2nd leading cause of cancer leading death
- Incidence in United States increasing due to chronic HCV
- Risk factors – cirrhosis!!
 - > 80% cases occur in setting of cirrhosis
 - 20% of patients with HCC and HBV do not have cirrhosis
 - Alcohol
 - Tobacco
 - Obesity
 - DM
 - Older age
 - Male gender



FLL – HCC (diagnosis)

- **Imaging!!** – arterial enhancement with “washout”
- **CT/MRI** should be performed when US shows FLL >1cm., elevated or rising AFP in absence of a FLL, when HCC suspected
- **CT vs. MRI** – several studies done and both acceptable
 - Use locally available expertise
- **When to biopsy?**



FLL – CCA

- Intrahepatic CCA accounts for 5-10% of all CCA
- Pt. with PSC have 1.5% annual risk of developing CA
 - 30% of those that do get CCA do so within 2 years of PSC dx.
- If FLL found in PSC pt., suspect CCA!!
- Other risk factors:
 - Tobacco
 - Alcohol
 - Age > 65
 - Liver fluke infestation
 - Caroli's disease
 - Choledochal cyst
 - Bile duct adenoma
 - Chronic intrahepatic stones
 - Chemical agents (vinyl chloride)
 - Cirrhosis



Opisthorchis viverrini



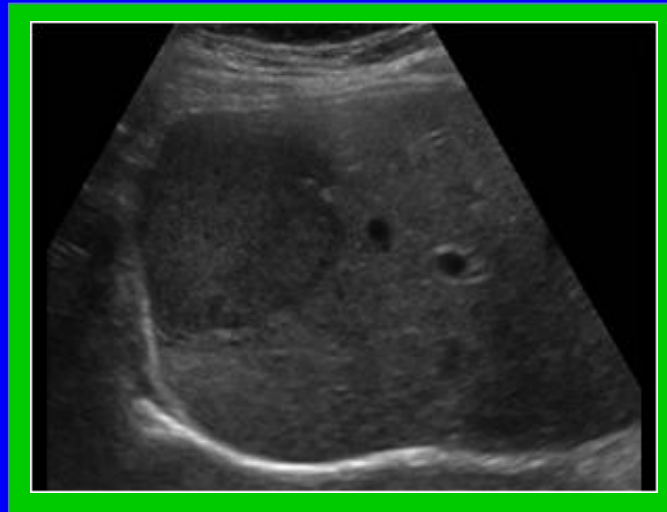
Clonorchis sinensis

FLL – CCA

- **Presents as painless jaundice most commonly**
- **1 and 5 year survival 27.6% and < 10%**
- **Diagnosis not made by imaging alone**
- **Biopsy usually needed to confirm diagnosis**
- **CT or MRI appropriate**
- **CA 19-9 elevated**
- **Treatment**
 - **Liver resection if none of the following are present**
 - **Extrahepatic metastasis**
 - **Main portal vein or hepatic artery invasion**
 - **Bilateral segmental bile duct involvement**
 - **Contralateral hepatic lobar atrophy**

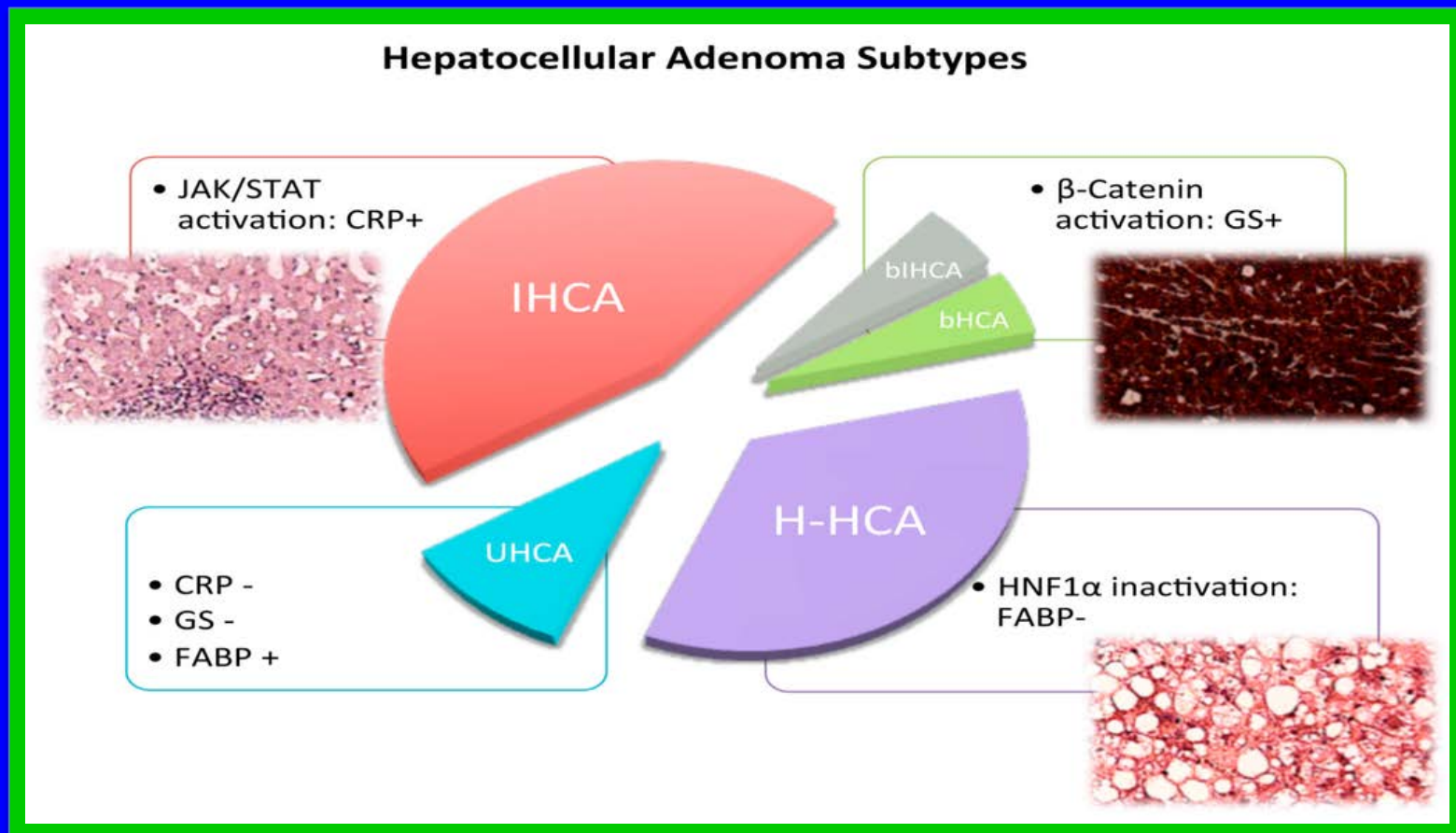
FLL – HCA

- **Benign neoplasm that arises *de novo***
- **Rare – 0.007-0.012% of pop. develops it**
- **Risk factors – OCP!!**
 - **1-1.3 per million vs. 34 per million**
 - **Tend to regress after OCP withdrawn**
 - **Anabolic androgens increase risk**
 - **Obesity and metabolic syndrome promote progression**
 - **Glycogen storage disease Ia and III**



FLL – HCA

- Liver adenomatosis – multiple adenomas
 - > 3
 - ≥ 10



FLL – HCA (diagnosis)

- Typically symptomatic, incidentally discovered 15-25%
- CT can be used but MRI preferred as it can identify HCA subtype
- HCA quite vascular making biopsy high risk to cause hemorrhage
 - Only used when imaging inconclusive AND it will have impact on therapy
- A word on pregnancy...
 - HCA increase in size during pregnancy
 - Infrequency of HCA has hindered an evidenced based approach to management
 - Pregnancy not discouraged if lesions < 5cm.



FLL – HCA (diagnosis)

- Treatment of HCA more aggressive than most benign FLL due to potential for hemorrhage OR progression to HCC
 - 11-29% HCA hemorrhage, nearly all of which are > 5cm.
 - Beta catenin subtype highest potential for malignant transformation
- > 5cm. – consider surgical resection
 - Embolization in high risk patients or anatomically difficult locations
- < 5cm. – conservative management
 - Follow-up imaging q6 months x2 years, then annual
- Avoid OCP and hormone containing IUD, DC if possible



FLL – Hemangioma

- Vascular lesions of unknown etiology, possibly related to congenital hamartomas
- Most common benign liver tumors
 - Prevalence – 0.4-20% during autopsy studies
- Most common in women (5:1)
- No causal link with pregnancy or OCP
 - Grow in size during pregnancy and on OCP



FLL – Hemangioma (dx.)

- Most discovered incidentally on imaging studies
 - Usually asymptomatic, only 11-14% have symptoms
 - RUQ pain
 - Epigastric mass
 - Nausea
 - Dyspepsia
 - Early satiety
- Secondary to compression and displacement of other structures
- Kasabach-Merritt syndrome – giant hemangiomas causing a consumptive coagulopathy
 - CT, MRI, and US effective for diagnosis
 - Peripheral enhancement
 - Progressive centripetal fill-in
 - Biopsy should be avoided due to high risk of bleeding

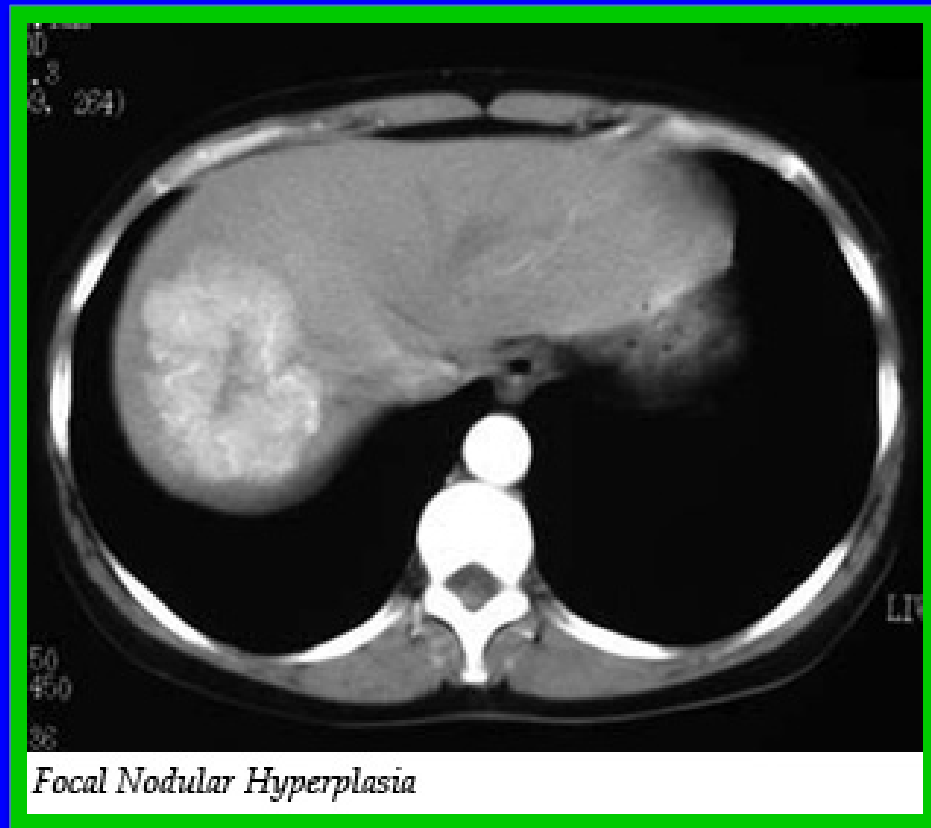
FLL – Hemangioma (tx.)

- Majority of hemangiomas are stable over time and asymptomatic
 - Surgical intervention typically not needed
- Surgical intervention indicated when lesion > 10cm. or symptomatic
- Follow-up imaging not required in cases of classic hemangioma



FLL – FNH

- 2nd most common hepatic lesion (0.3-3%)
- Development is caused by an injury to the portal tract resulting in the formation and enlargement of arterial to venous shunts
 - Leads to hyperperfusion in local arteries causing oxidative stress which causes “central scar” typical of FNH



FLL – FNH

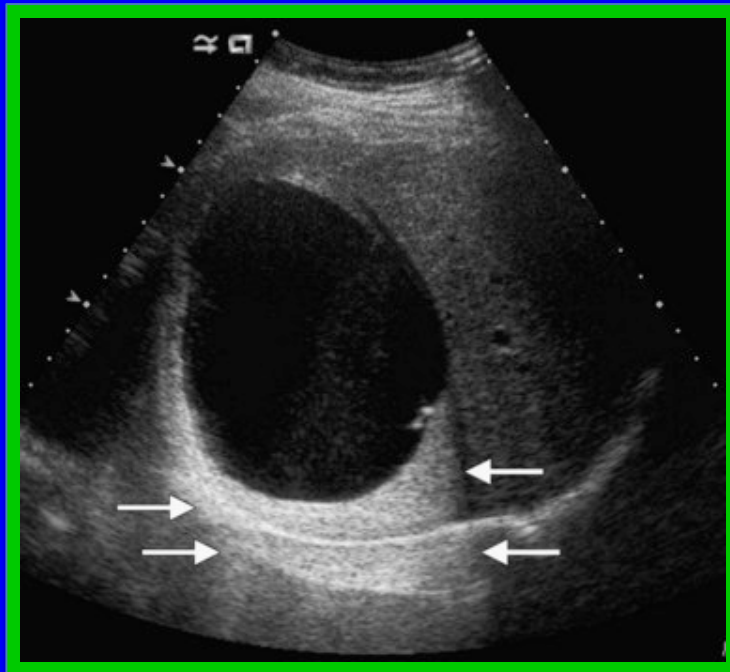
- **Most discovered incidentally**
- **20% associated with concomitant hemangiomas**
- **Primarily seen in women in 40's and 50's**
- **Not associated with pregnancy or OCP**
- **Diagnosed radiographically:**
 - **“spoke-wheel” central scar**
 - **Ambiguous cases must be differentiated from HCA, and if doubt persists after CT or MRI → biopsy!!**
- **Treatment:**
 - **Most are asymptomatic and stable over time, so conservative management recommended**
 - **Follow-up US in 2-3 years in women who continue OCP**
 - **Not needed if not on OCP**

FLL – hepatic cysts

- Typically found incidentally: 0.2-1% in early laparotomy studies
- Natural history not well elucidated, but not thought to be premalignant lesions
- Optimal management not clear due to lack of formal studies
- Several features warrant further evaluation:
 - Multiple cysts (>20)
 - Large cysts (> 4-5cm)
 - Septations
 - Calcifications
 - Loculation
 - Heterogeneity
 - Daughter cysts
 - symptoms

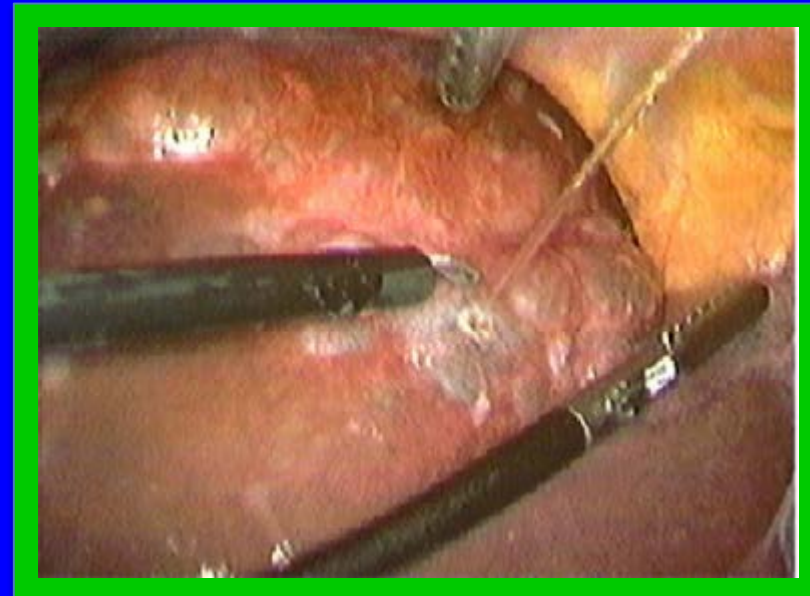
FLL – simple cyst

- Congenital exclusions of hyperplastic bile ducts that lack communication with bile duct
- Lined by columnar epithelium that produces cystic fluid
- Usually < 1cm but can grow to > 30cm
- Diagnosis:
 - US – anechoic, homogenous, fluid filled, smooth margins



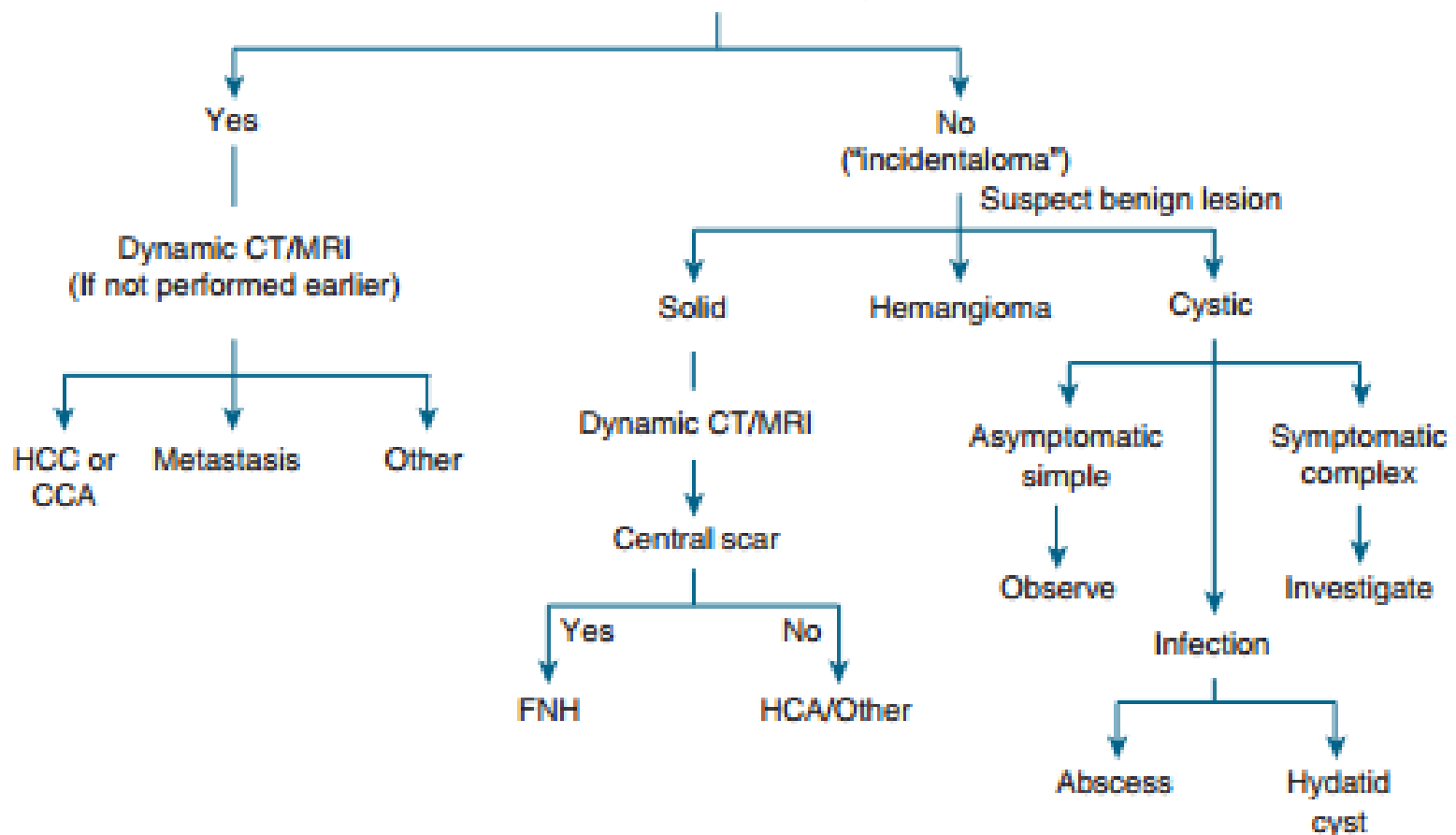
FLL – simple cyst

- **Management:** several basic dictums found in literature
 - Incidentally found, asymptomatic cysts do **NOT** need follow-up
 - Hepatic cysts that are symptomatic merit intervention
 - Simple aspiration is **NOT** recommended as it leads to universal recurrence
- If surgical candidate – open cyst fenestration (“deroofing”)
- If **NOT** surgical candidate – cyst aspiration followed by sclerotherapy



Approach to FLLs

Risk factors for HCC, H/O of malignancy
elevated tumor markers, weight loss



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