



# In Liver Transplant

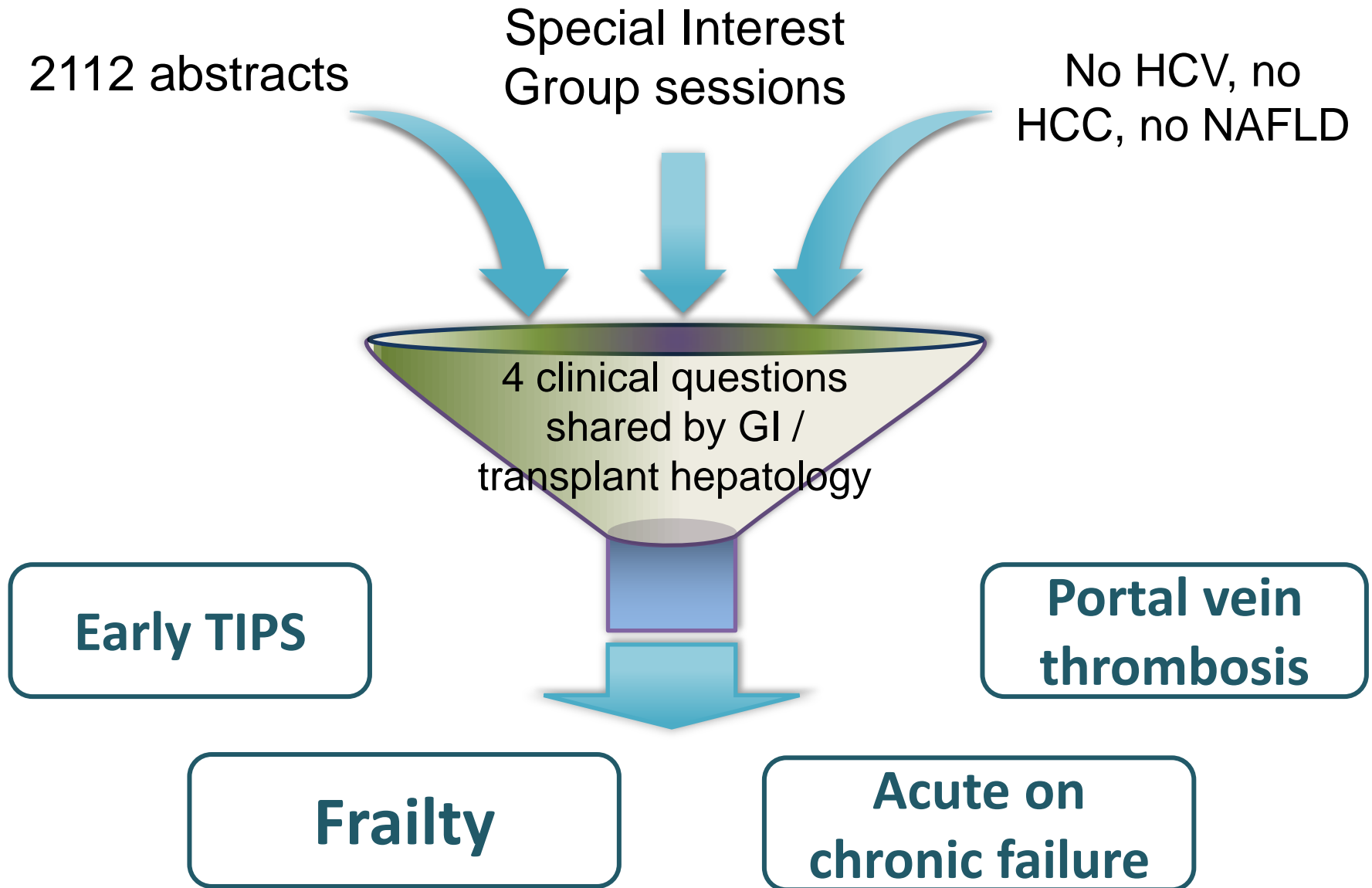


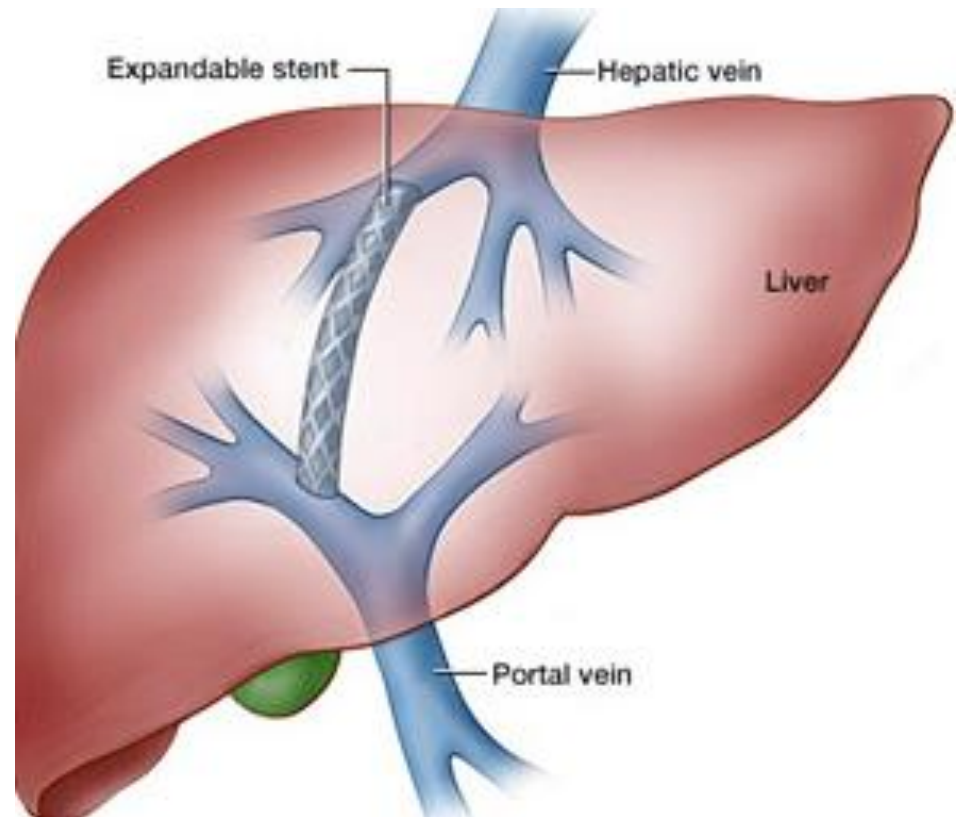
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NCSCG Post-AASLD Symposium

December 10, 2016

# AASLD Liver Meeting 2016





Early TIPS

**SHOULD PATIENTS WITH CHILD C  
CIRRHOSIS WITH ACUTE VARICEAL  
BLEED UNDERGO EARLY TIPS?**

# Early TIPS Improves Survival

## Rationale:

- 20% of pts with acute variceal bleed die in 6 wks
- Prior study has shown benefit of early TIPS, but not many CP-C pts

## Aim:

To evaluate benefit of early TIPS for acute variceal bleed in “high-risk” patients : age>75, Cr>3, CP score 13, or PVT

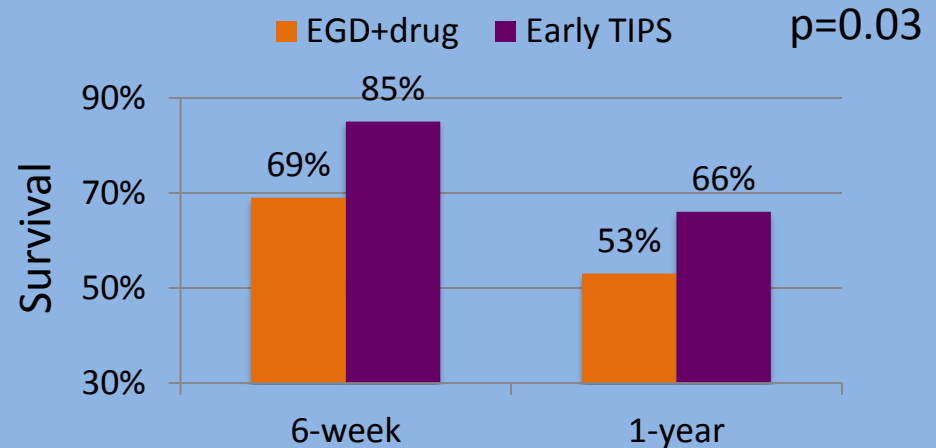
## Methods:

- Multi-center study:  
34 European ctrs,  
*retrospective* study  
underwent early TIPS

## Results

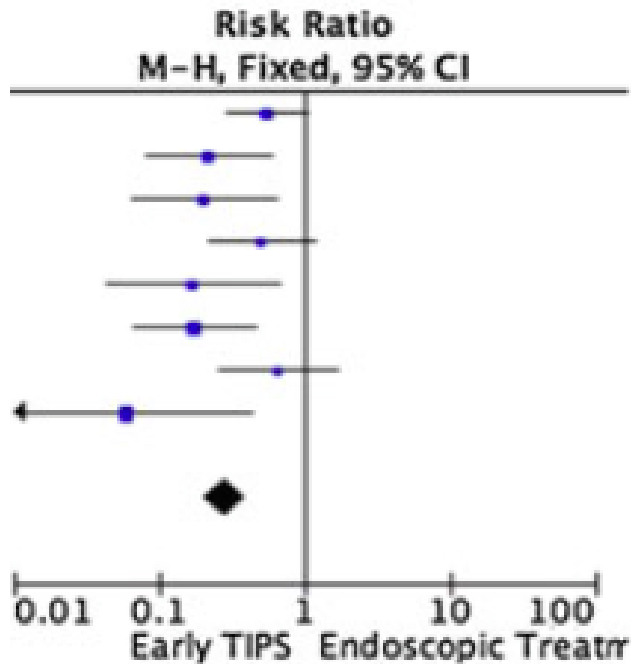
- 82 early TIPS
- 589 EGD + drug tx

} All “high-risk”  
Age>75 or Cr>3 or  
CP score>13 or PVT

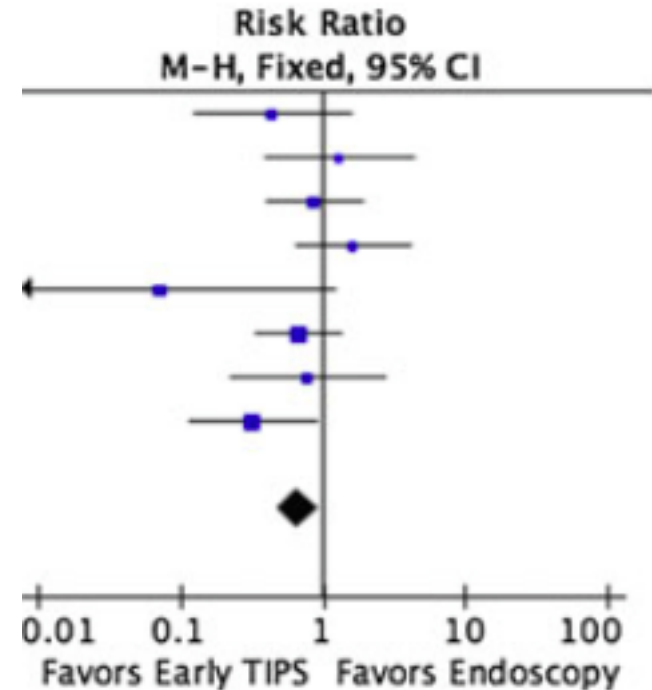


# Early TIPS for Acute Variceal Bleed: Meta-analysis

## Rebleeding @ 1-year

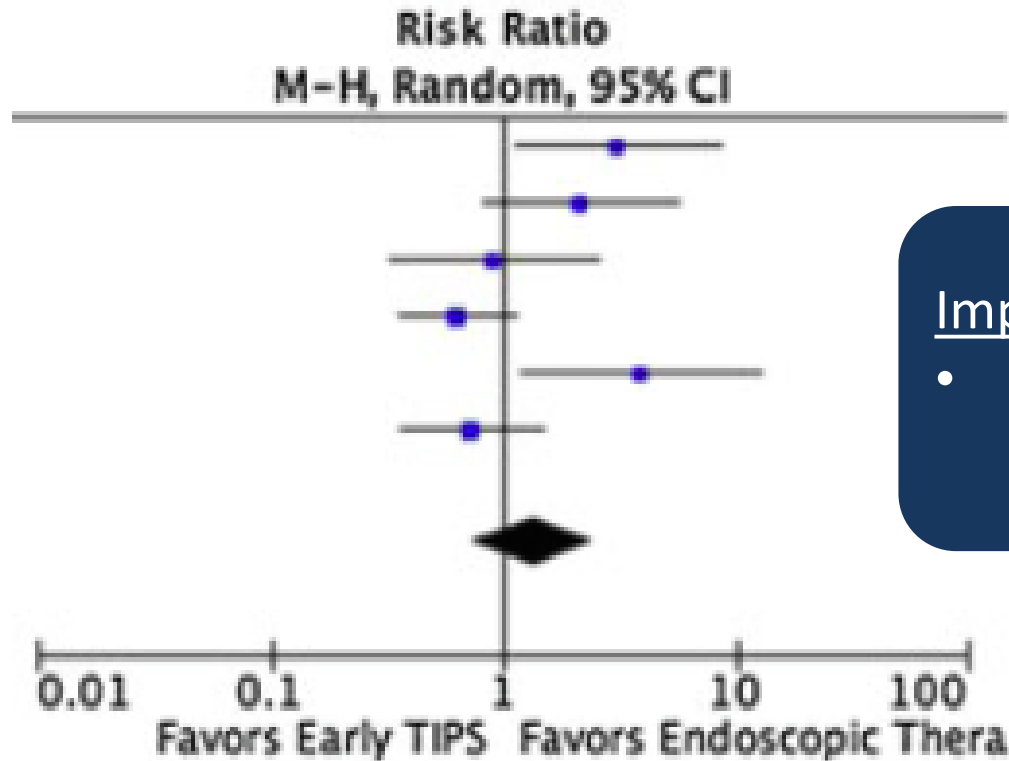


## Mortality @ 1-year



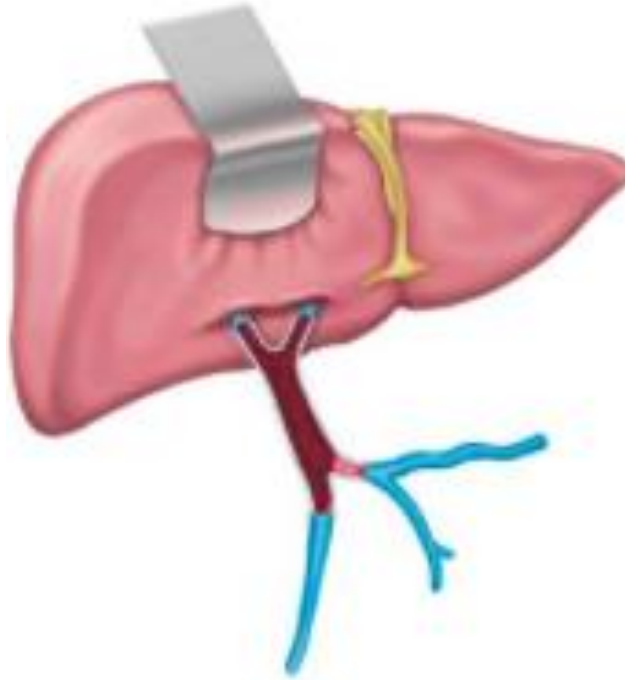
# Early TIPS for Acute Variceal Bleed: Meta-analysis

## Hepatic encephalopathy @ 1-year



### Implications for your practice:

- Refer all variceal bleeders for evaluation early TIPS



Portal Vein Thrombosis

**SHOULD CIRRHOTIC PATIENTS RECEIVE  
ANTICOAGULATION TO PREVENT PVT?**

# Enoxaparin prevents PVT and Liver Decompensation

70 pts with  
cirrhosis, no PVT

34 pt assigned  
to enoxaparin

36 pts assigned  
to no treatment

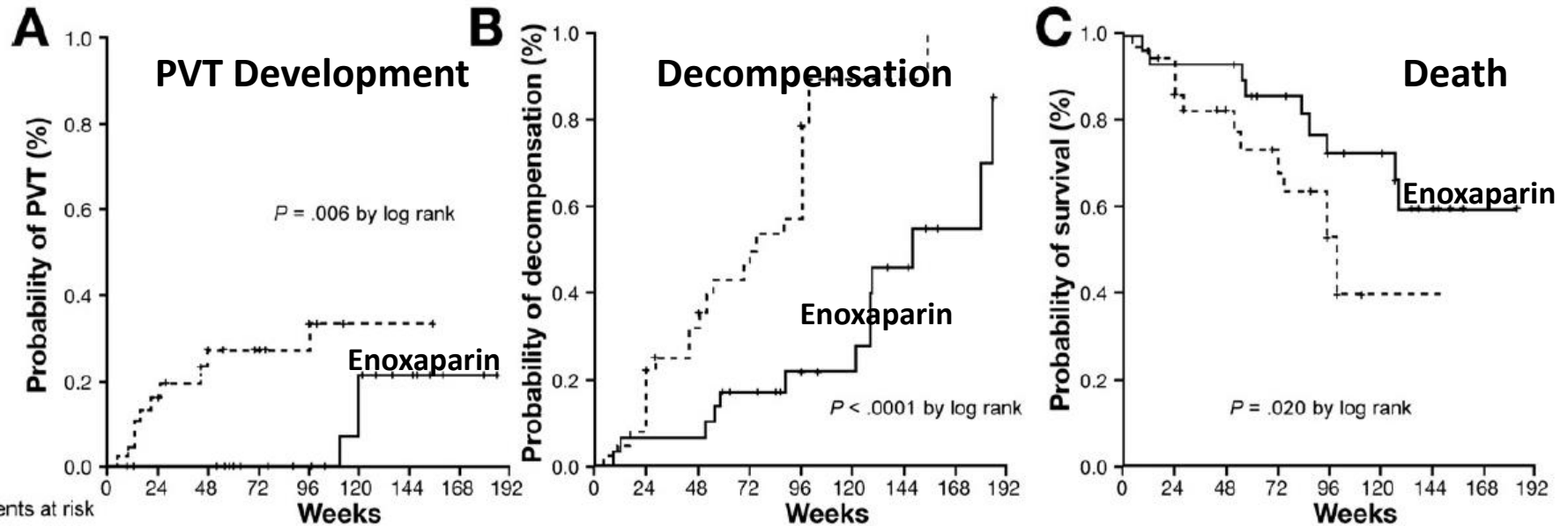
Baseline char.

Mean age ~57y

Child B (a few C)

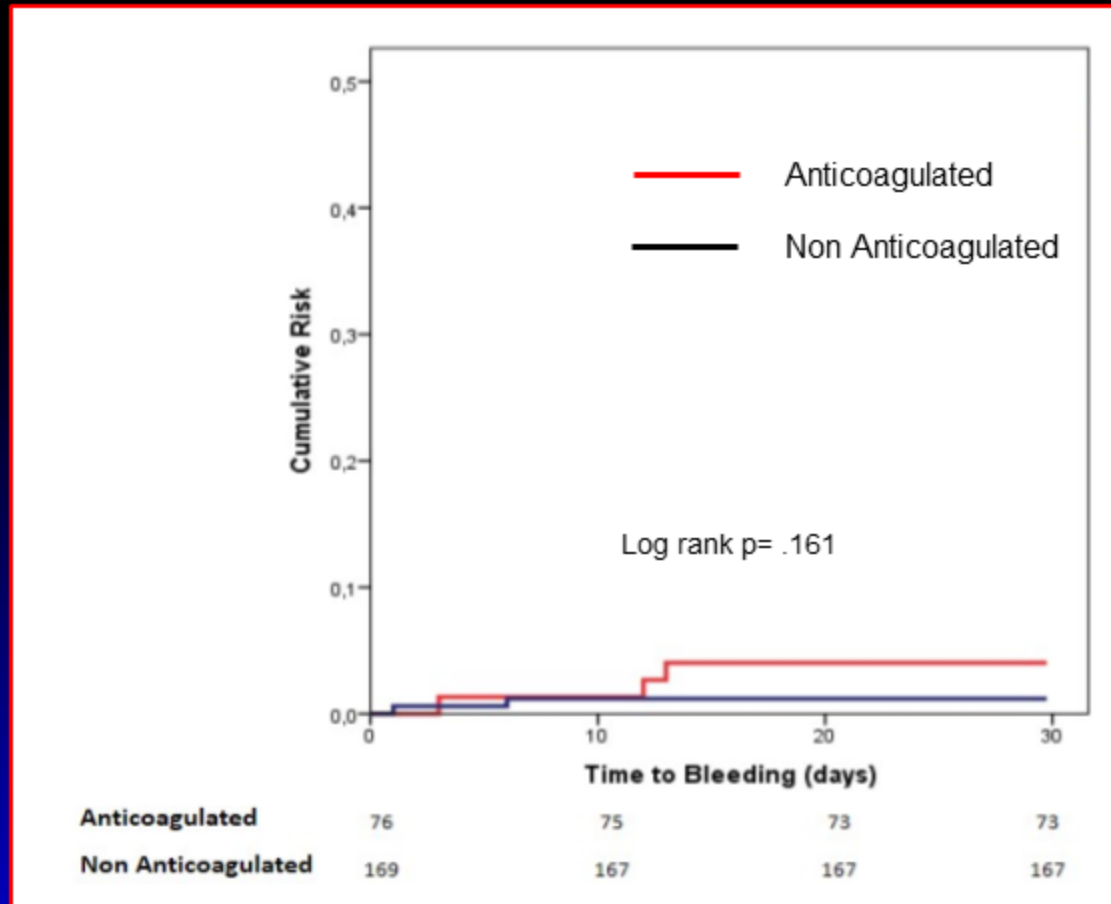
MELD~13

80% had varices





# LMWH does not increase the risk of bleeding after prophylactic endoscopic variceal band ligation in pts. with cirrhosis



Bianchini et al. EASL 2016

From Erica Villa, Portal HTN SIG AASLD 2016; data from Bianchini EASL 2016.

# Impact of anticoagulation on UGIB

Variable	Anticoagulated Patients (N = 52)	Non-anticoagulated Patients (N = 104)	P
MAP on admission (mmHg)	84 ± 15	80 ± 15	0.2
Hemoglobin on admission (g/dl)	10.4 ± 6.2	8.9 ± 2.1	0.08
RBC units transfused (N)	4.0 ± 2.8	4.8 ± 3.2	0.10
Active bleeding on EGD (%)	33	28	0.6
Failure to control bleeding 5d (%)	14	21	0.3
Mortality at 6 weeks (%)	8	17	0.8
Rescue therapy (%)	13	17	0.5

# Who will develop portal vein thrombosis?

## Rationale:

- Portal vein thrombosis (PVT) is associated with poorer overall outcomes
- Can be a contraindication to liver transplant

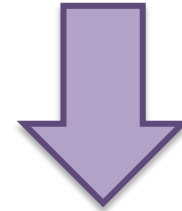
## Aim:

To identify predictors of developing PVT in patients with cirrhosis awaiting liver transplantation

## Methods:

- Single center study of patients with cirrhosis from 1987-2014
- Time from listing for LT to development of PVT

621 patients with cirrhosis listed for liver transplant



63 (10%)  
developed PVT

# Portal Vein Thrombosis Score

Risk  
factors:

Hepatic  
enceph  
HR 2.7

SBP  
HR 2.6

Gastro-  
EV  
HR 2.9

Total  
bili >4.5  
HR 3.9

PVT score	HR
0	Reference
1-2	3.2 (1.9-5.6)
3	15.5 (6.4-37.2)

## Implications for your practice:

- Consider anticoagulation in patients at high risk of PVT



Frailty / Sarcopenia

**WHAT IMPACT DO FRAILTY/ SARCOPENIA  
HAVE ON CIRRHOTIC PATIENTS? HOW CAN  
WE IDENTIFY FRAIL PATIENTS?**

# Sarcopenia as a predictor of mortality

## Rationale:

- Clinicians have long known that muscle wasting is an important prognostic indicator in cirrhotic patients
- The definition of “sarcopenia” has not been defined

## Aim:

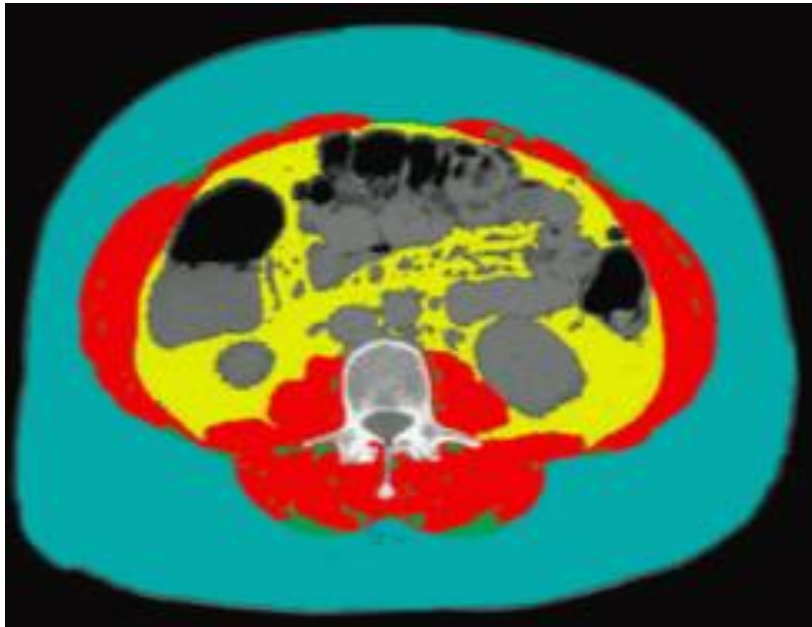
To define *sarcopenia* and quantify its impact on mortality in cirrhotic patients

## Methods:

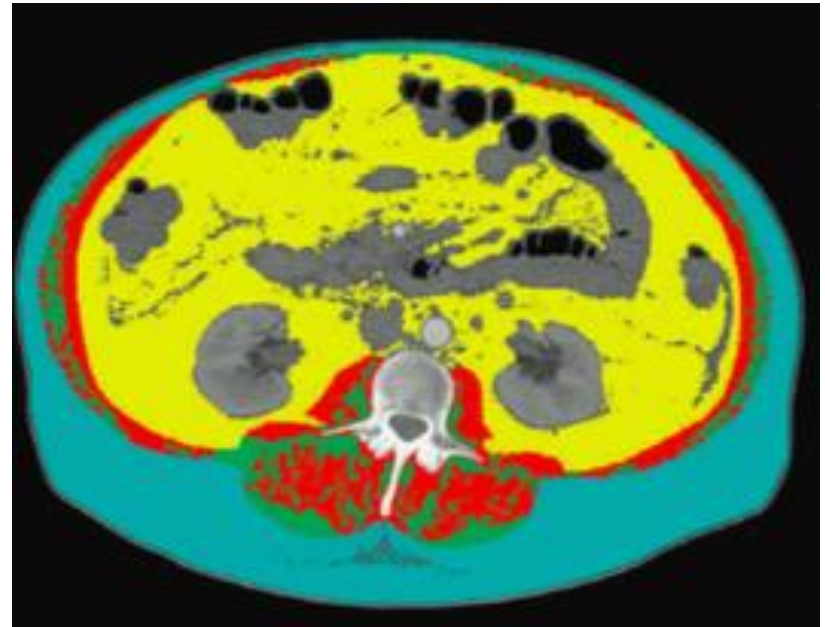
- ~400 liver transplant candidates
- **5 North American centers**
- Muscle mass quantified on CT scan

# Quantification of muscle mass (red)

## *Skeletal muscle index*



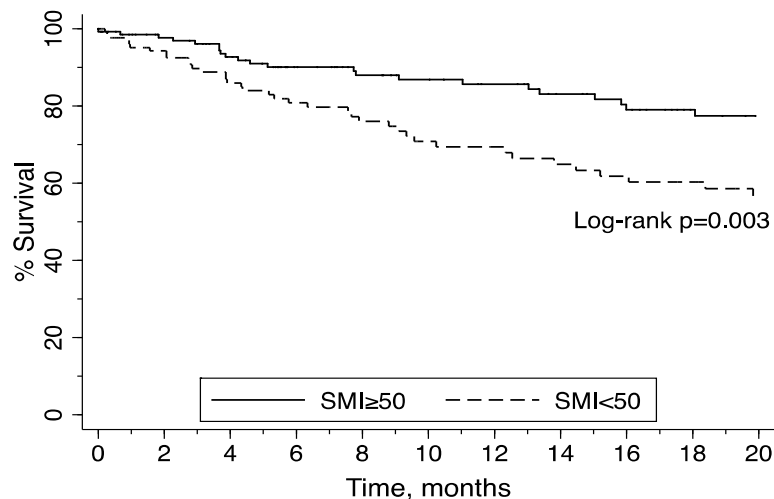
Normal muscle mass



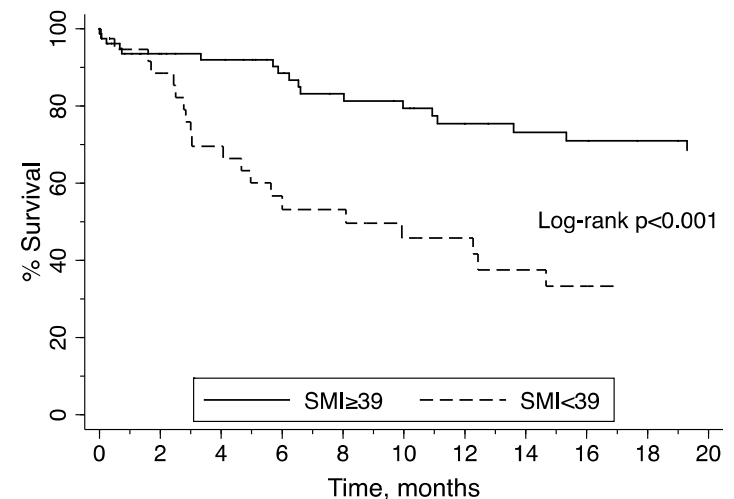
Low muscle mass

# Gender-specific cut-offs for sarcopenia predict waitlist mortality

Survival for **MEN** by skeletal muscle index  $< 50 \text{ cm}^2/\text{m}^2$



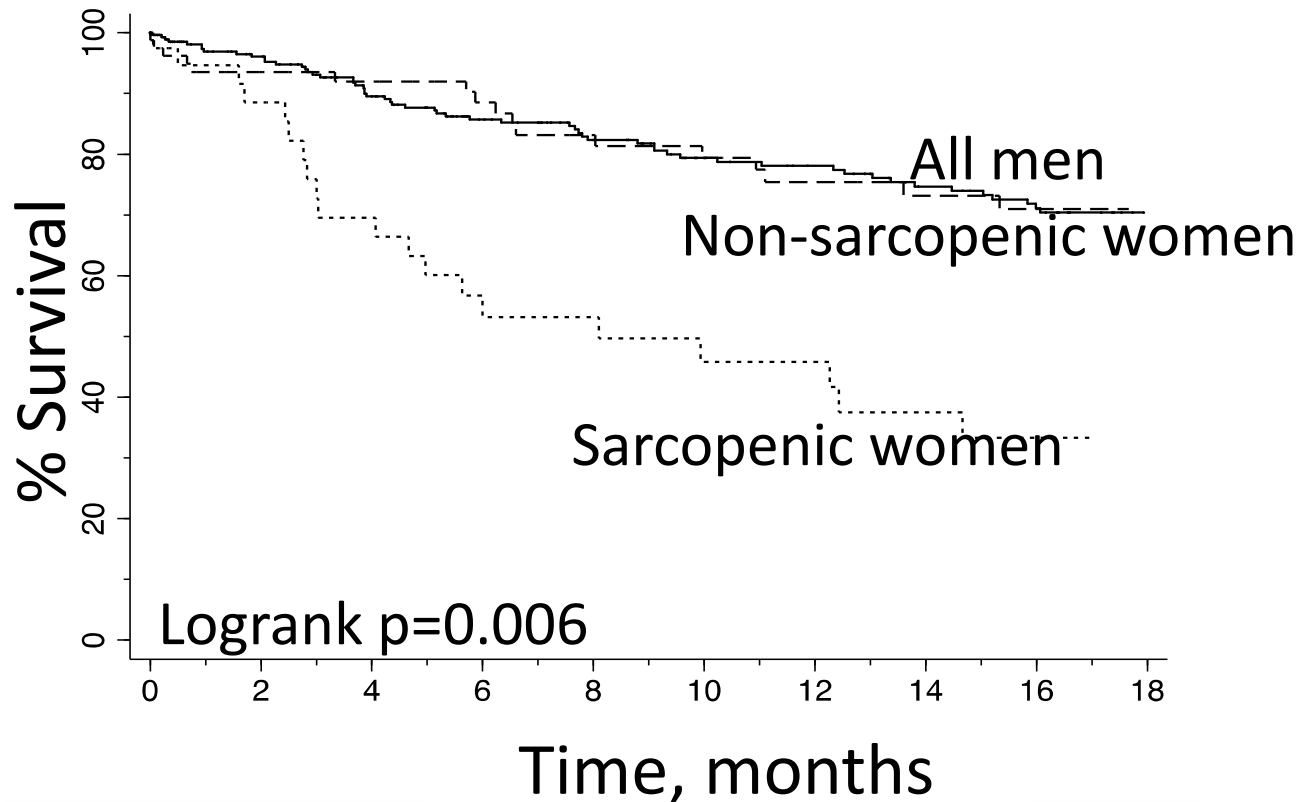
Survival for **WOMEN** by skeletal muscle index  $< 39 \text{ cm}^2/\text{m}^2$





# Sarcopenia accounts for gender difference in waitlist mortality

Unadjusted survival among men, non-sarcopenic, and sarcopenic women awaiting LT.



# Clinical Liver Frailty Index

## Rationale:

- We know when a patient is “frail”
- Clinical decision-making demands more objectivity

## Aim:

To develop an objective index to capture frailty that has prognostic value

## Methods:

- >500 LT candidates at UCSF undergoing frailty tests
- Excluded HCC
- Best subset selection

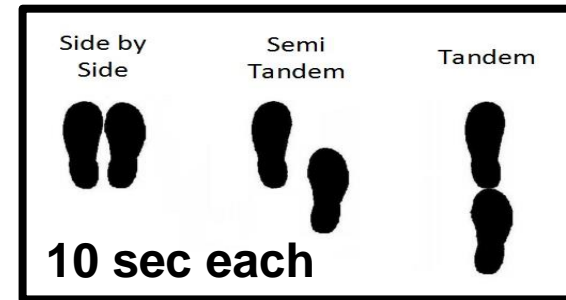


Functional Assessment  
In Liver Transplantation

# The Liver Frailty Index



$$\text{Grip}_{(\text{sex-adjusted})} * -0.330 + \text{Chair stands} * -2.529 + \text{Balance} * -0.040 + \text{constant}$$



Reclassification  
for waitlist  
mortality:

Frailty Index +  
MELDNa versus  
MELDNa alone

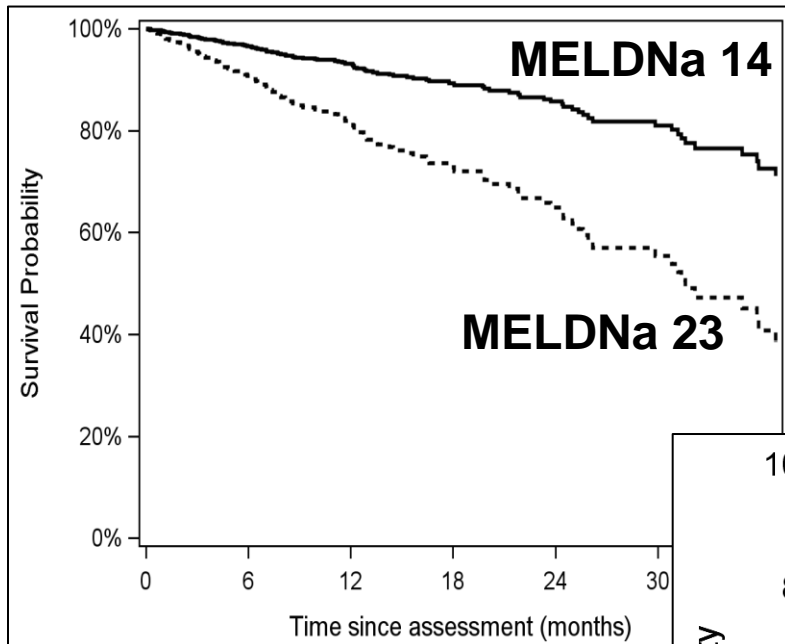
Deaths/delistings  
16%  
 $p=0.005$

Non-deaths/delistings  
3%  
 $p=0.17$



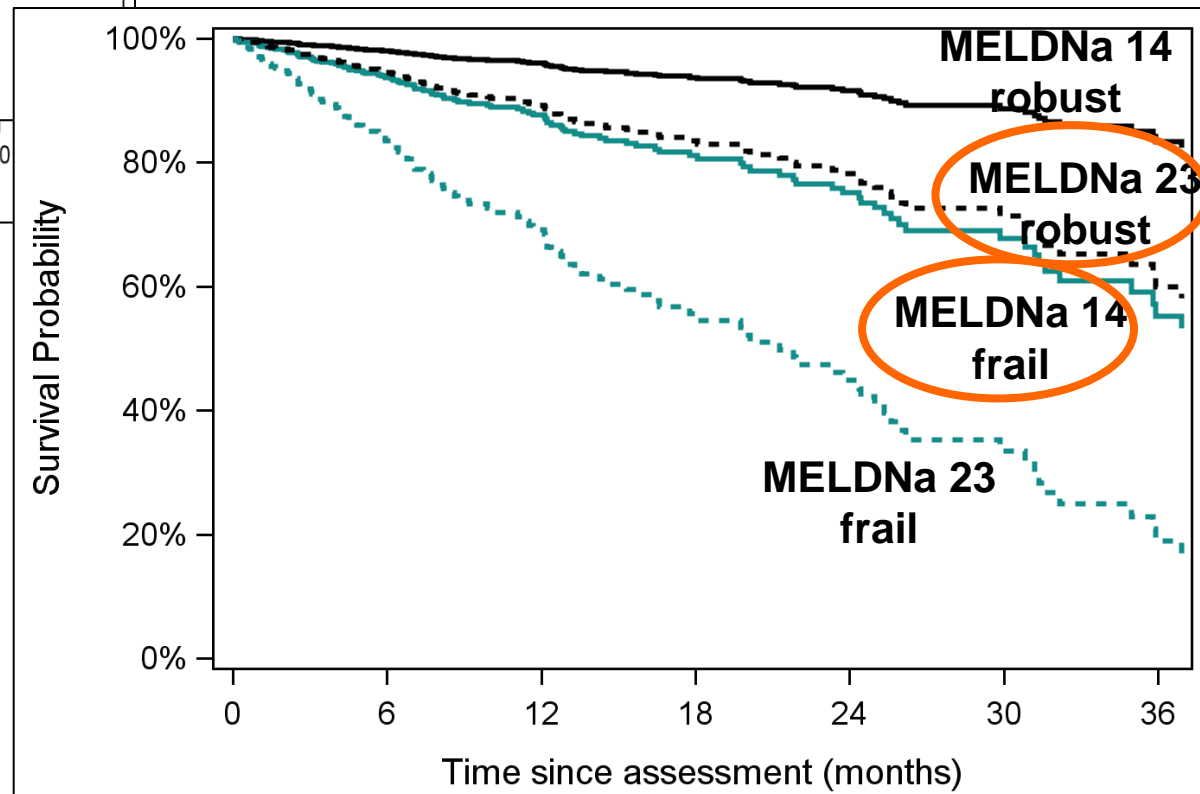
Net reclassification index  
19%  
 $p<0.001$

# Survival curves by MELDNa + LFI



## Implications for your practice:

- Cirrhotic patients with frailty / sarcopenia should be counseled on their high risk of mortality → need a faster path to transplant



# Transplant Futility

**Medical  
need**

**Probability of  
Restoration**

**Proceed with transplant?**

**MELD 40**

**PHTN  
complications**

**Frailty**

**Sarcopenia**



Critically ill cirrhotic patients

**SHOULD PATIENTS WITH ACUTE ON  
CHRONIC LIVER FAILURE UNDERGO  
LIVER TRANSPLANTATION?**

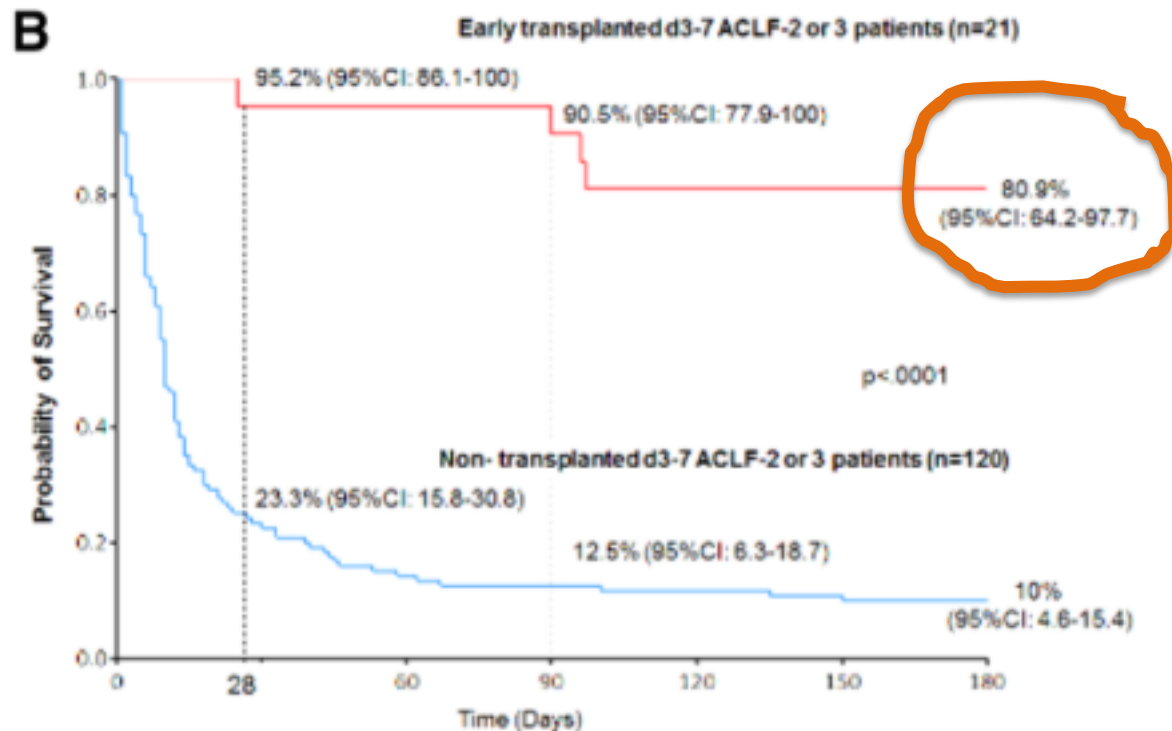
# Acute on Chronic Liver Failure: Consensus Definition

“A syndrome in patients with chronic liver disease with or without diagnosed cirrhosis which is characterized by acute hepatic decompensation resulting in:

- 1) Liver failure (jaundice + coagulopathy) *and*
- 2) One or more extrahepatic organ failures

That is associated with increased mortality within a period of 28-days to up to 3 months”

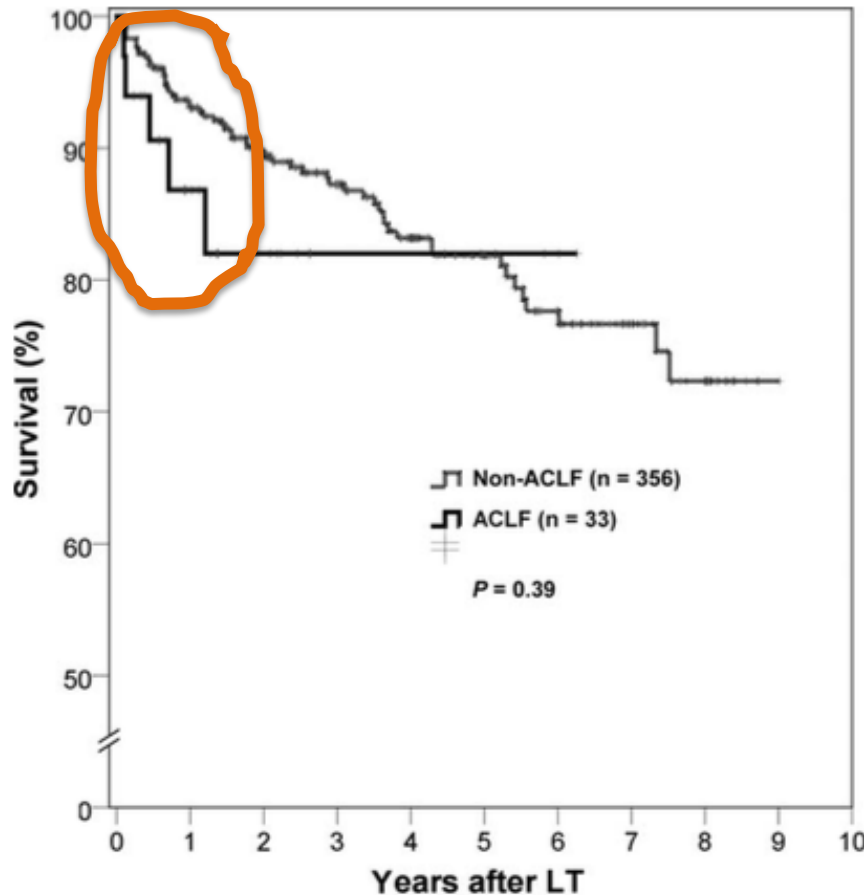
# Liver transplantation for ACLF: better survival W/ LT than W/O LT



Poor  
survival  
compared  
to non-ACLF  
recipients



# But worse than recipients who did not have ACLF at LT



## Causes of death in the ACLF group:

- Sepsis
- Secondary biliary cirrhosis
- Acute graft versus host disease

# Predicting 90-day mortality in LT recipients with ACLF

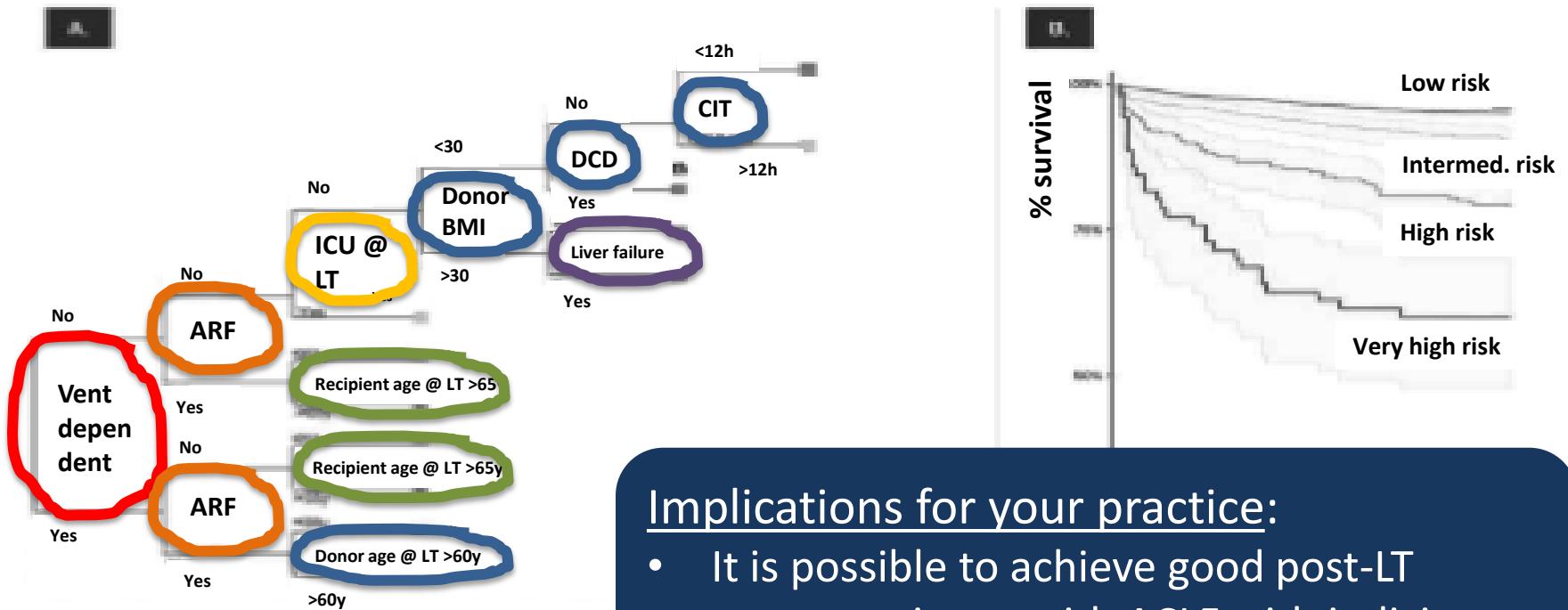
## Aim:

To build a decision-tree to predict 90-day mortality in LT patients with ACLF

## Methods:

- French national registry data
- n=1657 pts with ACLF
- CART modeling (machine learning)

Decision tree from CART survival analysis (A) and corresponding Kaplan-Meier curves (B)



## Implications for your practice:

- It is possible to achieve good post-LT outcomes in pts with ACLF with judicious selection of candidates and donors

# Key Points

Clinical question	Recommendation
Should patients with Child C cirrhosis with acute variceal bleed undergo early TIPS?	<ul style="list-style-type: none"><li>• Early TIPS in Child C patients reduces risk of re-bleeding and has modest (but statistically significant) impact on mortality</li></ul>
What impact do frailty/ sarcopenia have on cirrhotic patients? How can we measure these factors?	<ul style="list-style-type: none"><li>• Frailty and sarcopenia are critical determinants of mortality in cirrhotic patients.</li><li>• Sarcopenia: skeletal muscle index &lt;50 for men and &lt;39 for women</li><li>• Liver Frailty Index for functional measure</li></ul>
Should cirrhotic patients receive anticoagulation to prevent PVT?	<ul style="list-style-type: none"><li>• Yes, particularly among those at high risk for PVT: hepatic encephalopathy, SBP, gastroesophageal varices, TB&gt;4.5</li></ul>
Should patients with acute on chronic liver failure undergo liver transplantation?	<ul style="list-style-type: none"><li>• Yes, but with caution</li><li>• Low recipient risk: Age&lt;65, not intubated, no RRT</li><li>• Low donor risk: age&lt;60, BMI&lt;30, non-DCD</li></ul>

# Thank you

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