



ADVANCING GI PATIENT CARE 2022

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APRIL 23–24, 2022
SOUTHLAKE, TEXAS

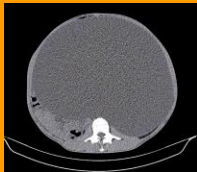


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Newly Diagnosed Cirrhosis

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Disclosures

- No relevant financial relationships to disclose.



Learning Objectives

“Apply optimal management strategies to prevent and minimize long-term complications of cirrhosis...”



Referred From PCP for Newly Diagnosed Cirrhosis

55 yo WM with DM, obesity
AST 50, ALT 38, TB 1.1, Plt 110

US – “cirrhotic” appearing liver

What are the next best steps?

Overview – 5 W's + H

Why?

Who & Where?

What? (Diagnosis)

How? (Management)

When? (Prognosis)

Why?

At risk for
decompensation,
liver cancer (HCC)

Associated with
reduced survival ~
12 years

1.32 M cirrhosis
related deaths/yr
worldwide~ (2.4%)

↑ # of cirrhotics
requiring GI care
~ 4 M with liver
disease in US

Who & Where in the Era of Personalized Medicine?

Who

Audience

- GI provider
- NOT transplant hepatologists
- NOT primary care providers

Patient before you:

- Individualized care
- Risk stratification
- Value/Outcome based care



Where

- Outpatient clinic

What Is Cirrhosis?

Structural – replacement of liver tissue by fibrous scar tissue, regenerative nodules

Functional – increase in hepatic vascular tone

Inflammation

Look for & **Confirm** the Diagnosis

What – Etiologies?

Treatable – HCV, PBC, AIH, HBV
Hemochromatosis, Wilson

Common – NAFLD
ETOH

Misc. – PSC, A1AT, BCS
Secondary Biliary, Cardiac

What – Decompensation?

Ascites

Variceal
Bleeding
(PVT)

Hepatic
Encephalopathy

Hepatocellular
Carcinoma

Jaundice

SBP,
Hepatorenal
Syndrome,
Hydrothorax

What – Diagnosis

Gold Standard = Liver Biopsy
(Yet limited by sampling error, Risks)

Serologic Markers
of Fibrosis:

APRI, FIB-4, Fibrotest,
Fibrosure, Actitest

Imaging,
Elastography

What – Indirect & Direct Markers of Fibrosis

APRI

AST, PLT
> 1 ~ 76% Sn
72% Sp for cirrhosis

FIB-4

Plt, AST, ALT, Age
> 3.25 ~ 97% Sp
67% PPV for cirrhosis

Fibrotest
Fibrosure

ActiTest
Hepascore

Good ability to differentiate significant fibrosis (F2-4) vs. those without (F0-1)
But not as good as distinguishing b/w stages, and indeterminate results are common

What – Imaging & Elastography

- US, CT, MRI
- Nodular Liver
- Caudate lobe enlargement
- Varices, portal HTN

- Transient Elastography
- MR Elastography

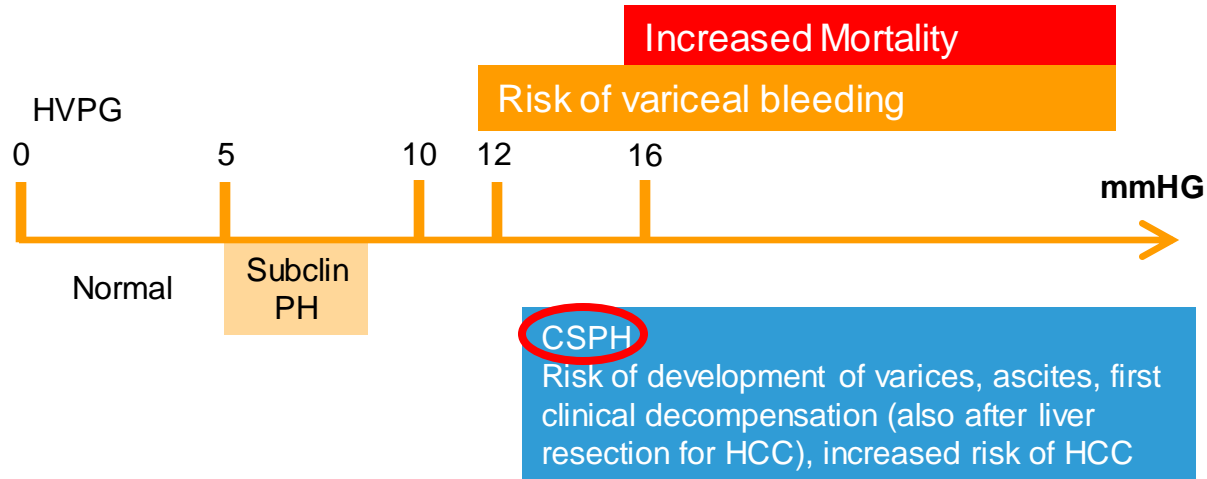
Always need to interpret the data in **CONTEXT**
of the clinical presentation

What – Staging

	F1-F3		F4 (Cirrhosis)	
Histological	← F1-F3 →		F4 (Cirrhosis) →	
Clinical	<i>Non-cirrhotic</i>	<i>Compensated</i>	<i>Compensated</i>	<i>Decompensated</i>
Symptoms	None	None (no varices)	None (varices present)	Ascites, VH Encephalopathy
Sub-stage	—	Stage 1	Stage 2	Stages 3 and 4
Hemodynamic (HVPg, mmHg)		>6	>10	>12
Biological	Fibrogenesis and Angiogenesis	Scar and X-linking	Thick (acellular) scar and nodules	Insoluble scar

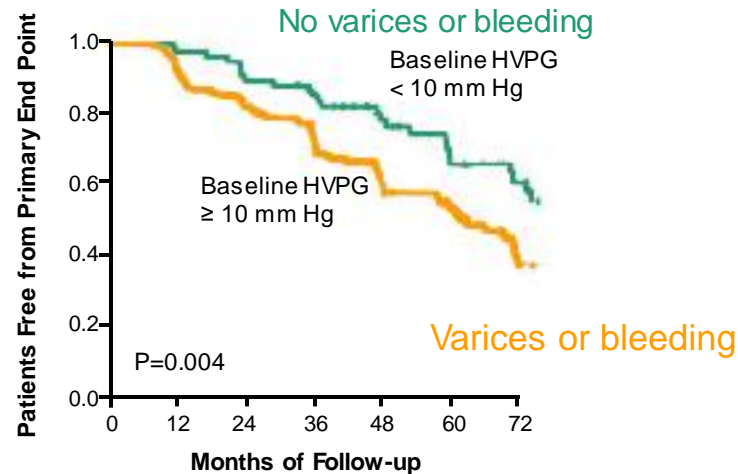
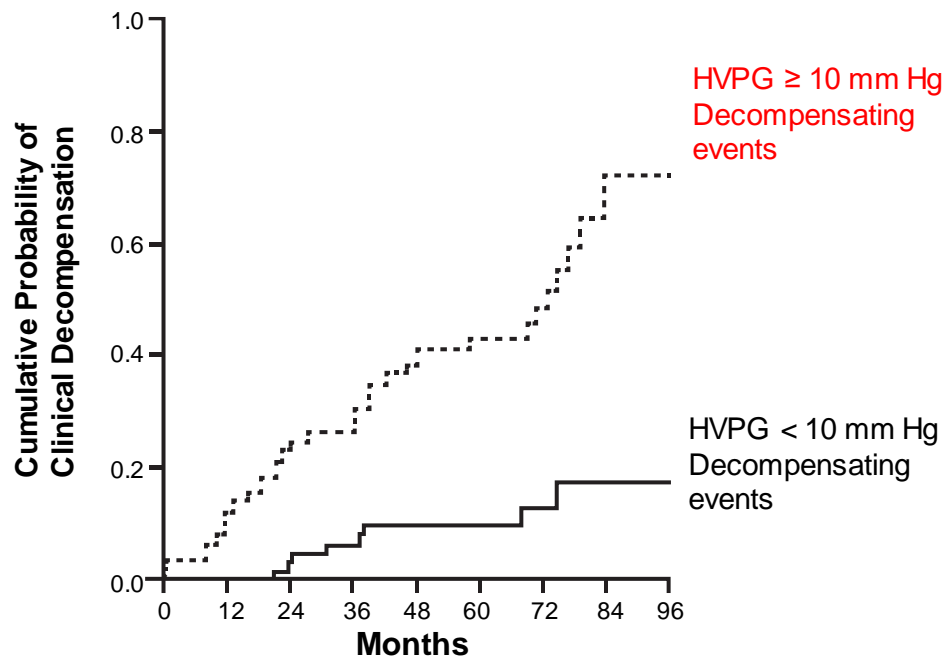
What – Clinically Significant Portal Hypertension ~ Detected by HVPG

Relevant thresholds of HVPG in compensated cirrhosis (target population)



HVPG: independently associated with prognosis in cirrhosis.

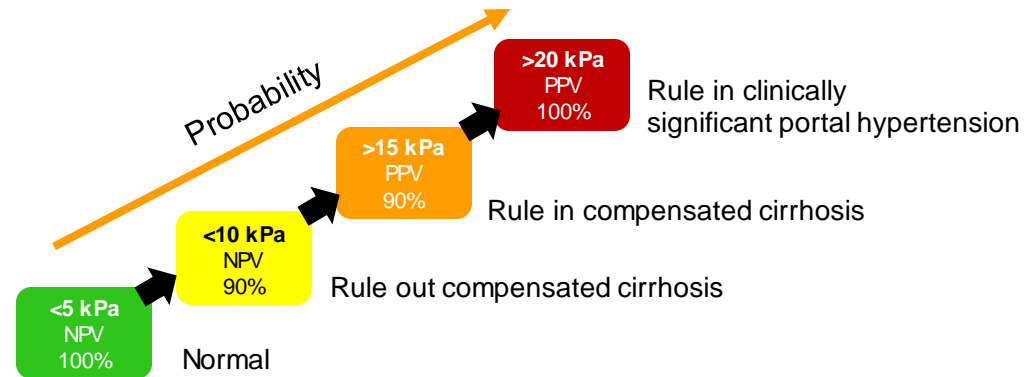
What – CSPH (Inc HVPG) Predicts Hepatic Decompensation



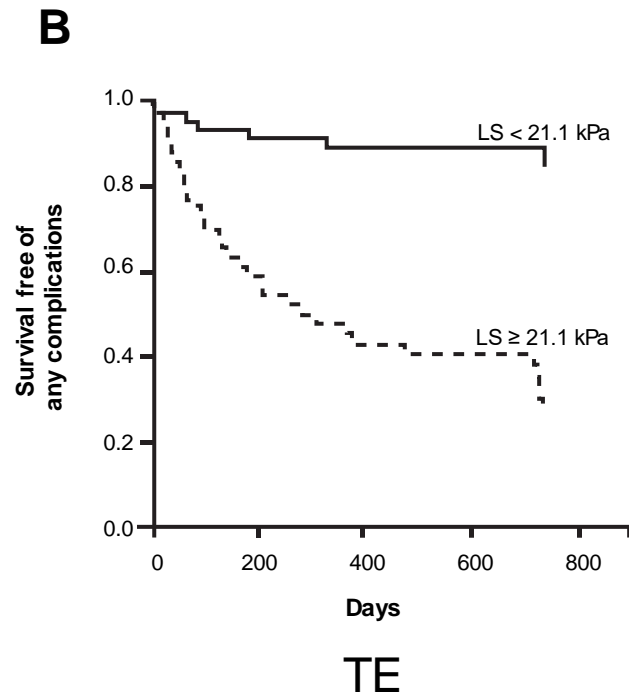
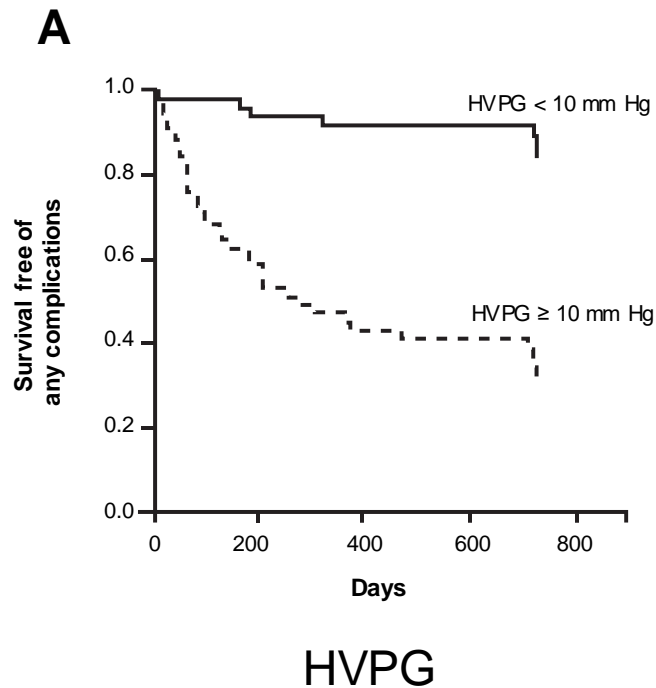
No. at Risk	0	12	24	36	48	60	72
HVPG ≥ 10 mm Hg	134	120	96	78	48	36	14
HVPG < 10 mm Hg	79	74	67	58	41	32	24

What – Transient Elastography (TE)

- Developed to assess hepatic fibrosis
- Can be used to predict CSPH
 - TE \geq 20 kPa + Plts \leq 150 or
 - TE \geq 25 kPa
 - Impractical to do HVPG broadly



What – TE Predicts Hepatic Decompensation



Outpatient Management

Etiological Testing- negative

APRI= 1.25, FIB-4= 4.06

US Elastography- cirrhotic appearing liver, 22 kPa=F4= **CSPH**

Liver Biopsy deferred by patient

What are the next best management steps?

How – Management?

Treat the underlying chronic liver disease
& Monitor for complications

Detect & Manage CSPH

HCC
Surveillance

Preventive
Care

Set Prognosis
Expectations
Early

Liver Transplant
Referral

How – Preventive Care

Dx & Rx
Cause:

HBV, HCV, AIH, PBC,
HH, WD, NAFLD, PSC

ETOH
Avoidance

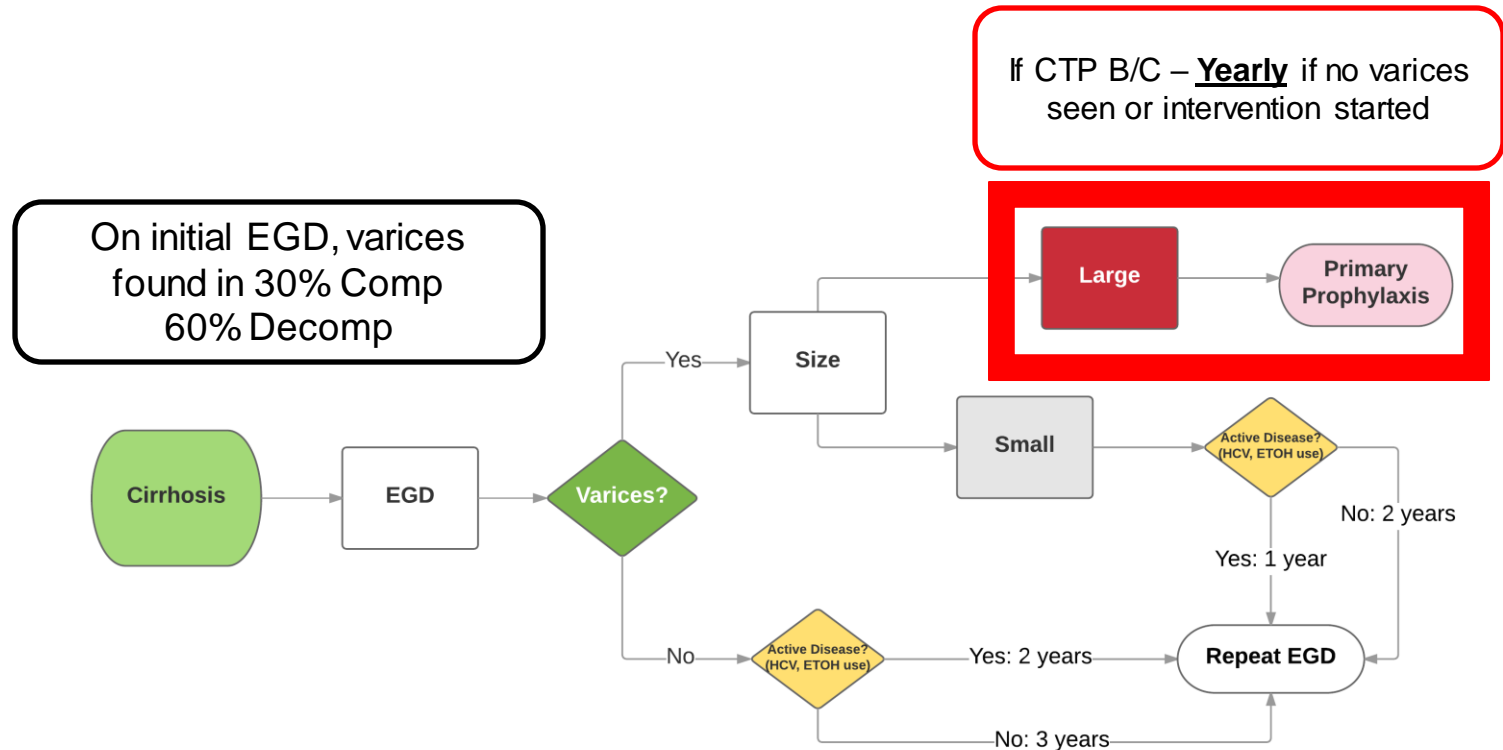
Nutrition:
Avoid High &
Very Low BMI

APAP > NSAIDs
Statins ok
Herbals
CNS acting Rx

BMD q 2-3y
Dental Care
Tobacco

Vaccinations
HAV, HBV
Flu, Pneumo.
Covid-19

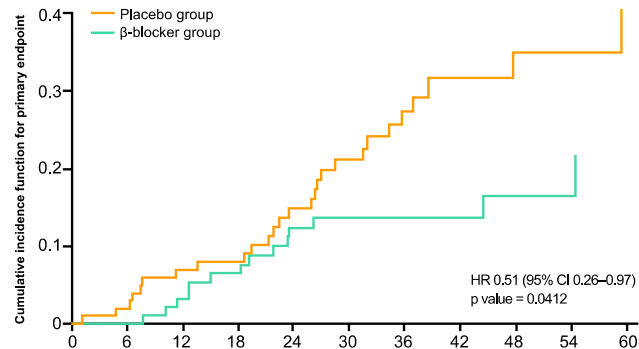
How – Old School Dx of CSPH



How – NSBB for CSPH

PREDESCI study

- RCT – BB to prevent decompensation in CSPH
- HVPG ≥ 10 mm Hg
- Propranolol/Carvedilol vs. Placebo



	Placebo group (n=101)	β -blockers group (n=100)	Risk (95% CI)*	p value†
Decompensation or death				
Overall‡	27 (27%)	16 (16%)	0.51 (0.26–0.97)	0.0412
Secondary outcomes				
Ascites	20 (20%)	9 (9%)	0.42 (0.19–0.92)	0.030
Gastrointestinal bleeding	3 (3%)	4 (4%)	1.52 (0.34–6.82)	0.61
Overt hepatic encephalopathy	5 (5%)	4 (4%)	0.92 (0.40–2.21)	0.98
Death from any cause	11 (11%)	8 (8%)	0.54 (0.20–1.48)	0.23
Varices	56 (56%)	58 (58%)	1.15 (0.65–2.02)	0.72
High-risk varices§	25 (25%)	16 (16%)	0.60 (0.30–1.21)	0.15
Spontaneous bacterial peritonitis	4 (4%)	2 (2%)	0.49 (0.10–2.70)	0.40
Other bacterial infections¶	19 (19%)	15 (15%)	0.81 (0.41–1.59)	0.54
Hepatorenal syndrome	1 (1%)	1 (1%)	0.99 (0.06–15.96)	0.96
Hepatocellular carcinoma	17 (17%)	13 (13%)	0.76 (0.37–1.54)	0.43

How – Carvedilol

Meta-analysis of individual patient data



only patients without any previous decompensating event
included to pool the individual data



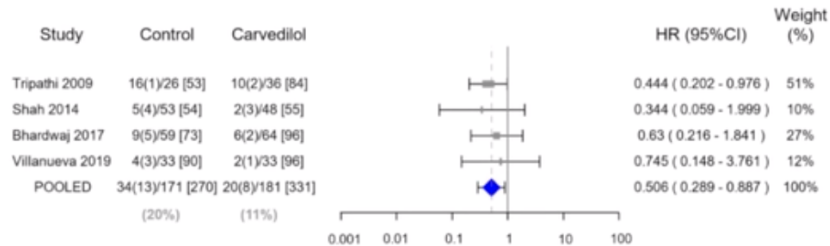
PRIMARY OUTCOME MEASURES

- * Development of cirrhosis decompensation (ascites, PH-bleeding, overt HE)
- * Death from any causes

How – Carvedilol prevents Decompensation + Death

Primary Outcome : Decompensation

DEATH & LT AS COMPETING EVENTS



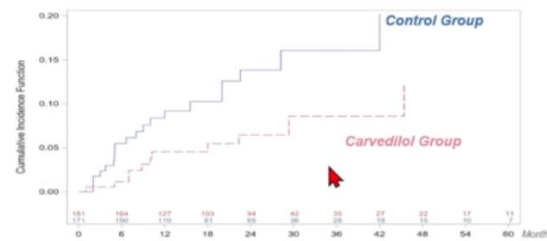
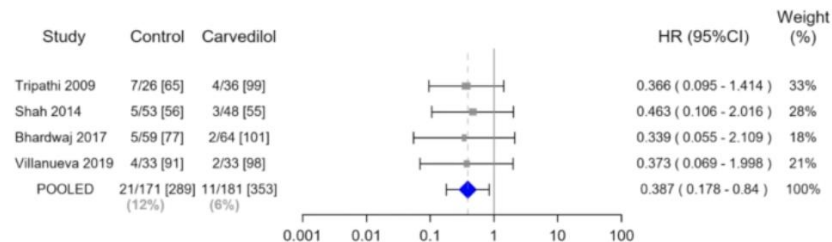
SHR= 0.506 (95%CI= 0.289-0.887)
Pvalue= 0.017

ADJUSTED FOR RISK FACTORS
(Child-Pugh, etiology, Hemoglobin)
SHR= 0.466 (95%CI= 0.268-0.813)
Pvalue= 0.007

Villanueva et al ILC 2021

Primary Outcome : Death, all causes

OLT AS COMPETING EVENT



SHR= 0.477 (95%CI= 0.230-0.988)
P-value= 0.016

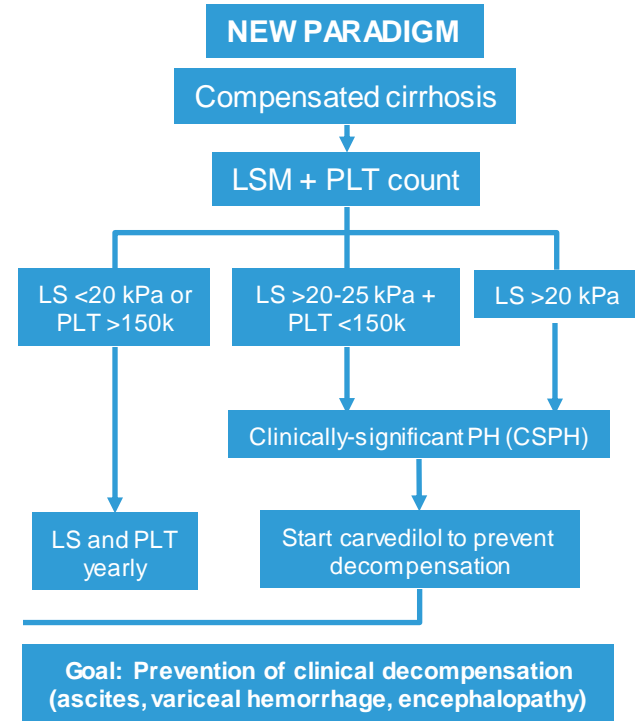
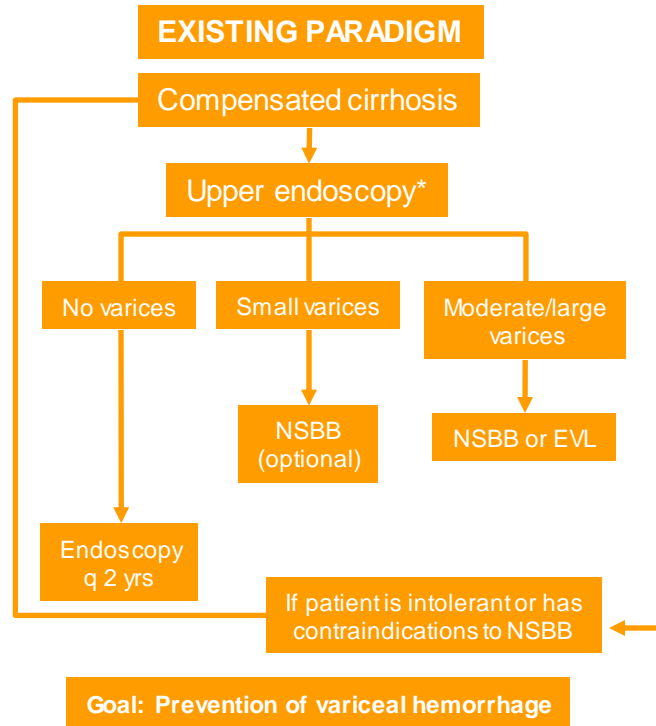
ADJUSTED FOR RISK FACTORS
(Child-Pugh, etiology)
SHR= 0.417 (95%CI= 0.202-0.858)
P-value= 0.017

Villanueva et al ILC 2021

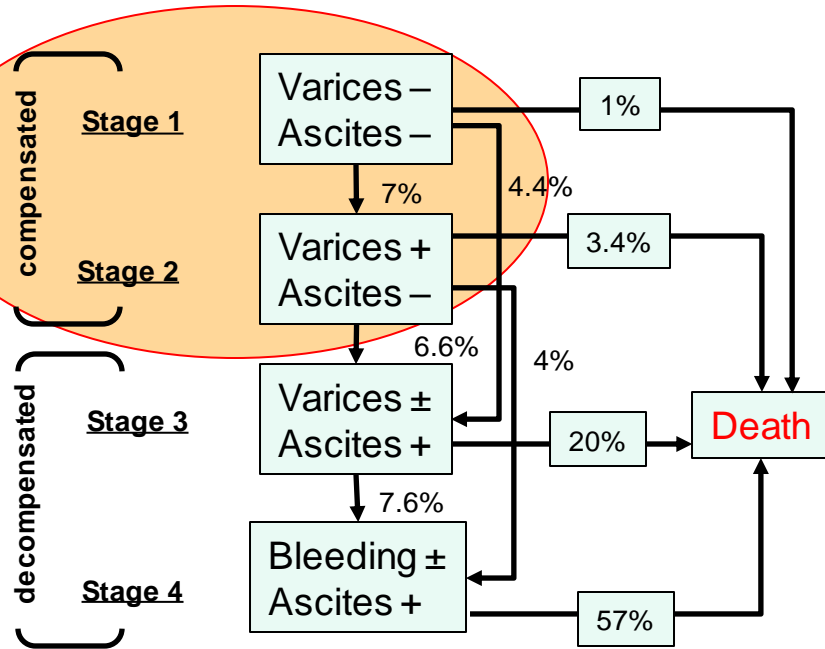
How – Guidelines Changes Coming

	Baveno VI (2015)	Baveno VII (2021)
Compensated cirrhosis, No CSPH TE < 20 kPa Plt > 150,000	No screening EGD needed; repeat testing yearly	<u>No screening EGD</u> needed; repeat testing yearly
Compensated cirrhosis, CSPH TE ≥ 20 kPa and Plt ≤ 150,000	<u>Do EGD for varices screening</u>	
No varices/small varices CTP A-B	Repeat EGD 2 yrs	
Small varices, CTP C	Start NSBB	
Large varices	NSBB <u>or</u> EBL	

How – Paradigm Shift



When? Prognosis Defined by Decompensating Events



Median survival in:

- Compensated cirrhosis = 12-20 y
- Decompensated cirrhosis = 1/2- 2 y

Long Term Follow Up

CSPH Dx → Carvedilol initiated at 3.125 mg BID
→ 6.25 mg BID as tolerated

Q 6 mo- Labs + US + AFP

Prognosis & Liver Transplant Referral
Process Discussion

Take Aways

Why? *Cirrhosis is common and leads to death*

Who & Where? *Practicing GI in outpatient*

What? *Make the cirrhosis Dx, Evaluate for CSPH*

How? *Carvedilol, Rx underlying cause, Preventive care*

When? *Have the Prognosis discussion early*



Give thanks. Give life.