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Gastroenterological Society of Australia

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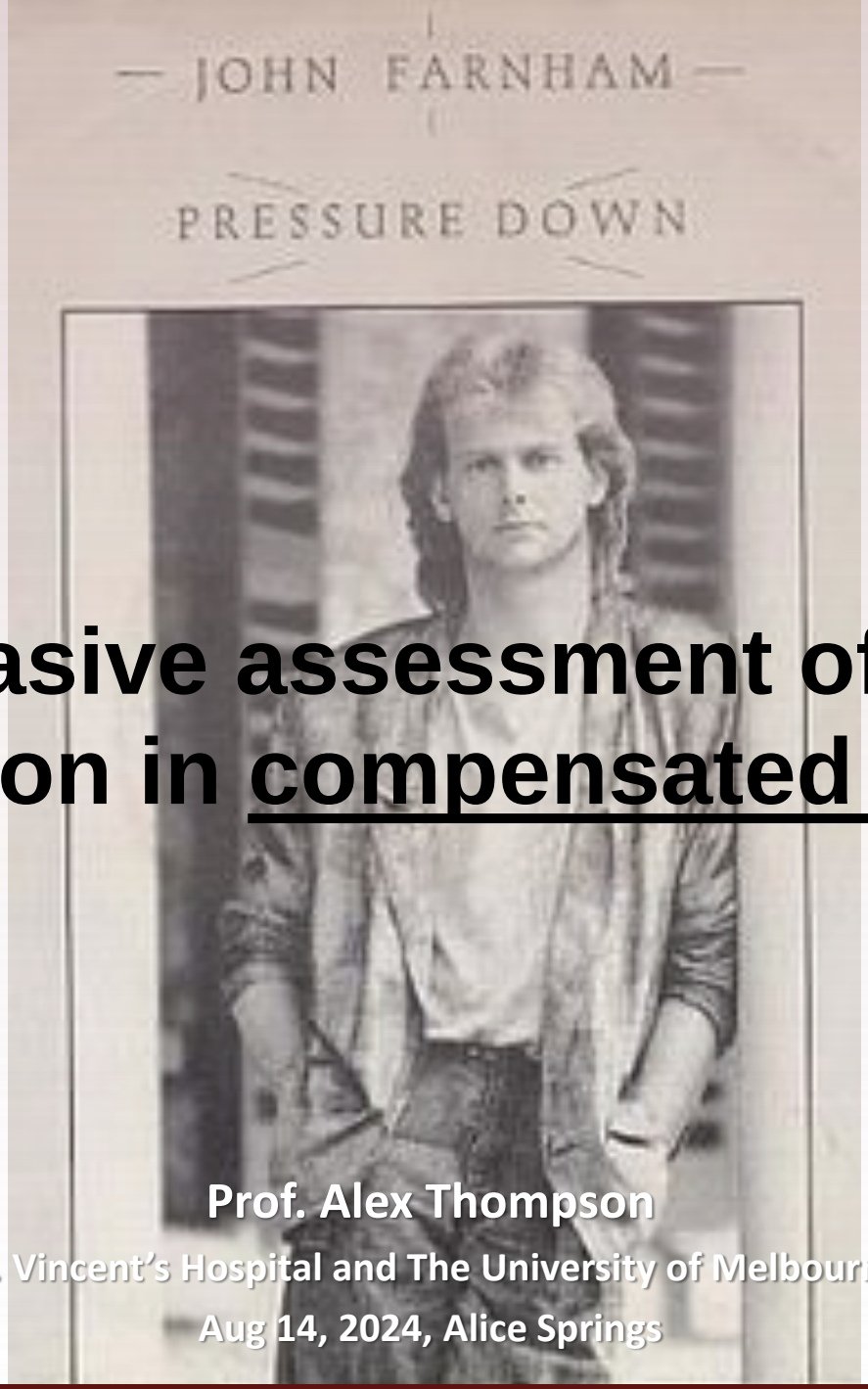
GUT CENTRE

13 - 16 August 2024
Alice Springs Hospital

The epicentre of gastrointestinal and liver education in Australia



Non-invasive assessment of portal hypertension in compensated cirrhosis

Prof. Alex Thompson

St. Vincent's Hospital and The University of Melbourne

Aug 14, 2024, Alice Springs

ACKNOWLEDGEMENT OF COUNTRY

- I begin today by acknowledging the Arrernte people, the traditional custodians of Mparntwe, the land on which we meet today, and pay my respects to their Elders past and present.
- I extend that respect to all Aboriginal and Torres Strait Islander peoples here today.

DISCLOSURES

- Consulting
  - Abbvie, Gilead Sciences, Assembly Biosciences, Roche Moelcular Systems
- Speaker
  - Roche Diagnostics, Roche, Abbvie, Gilead Sciences
- Research / grant support
  - Gilead Sciences, Abbvie, Roche Diagnostics

Agenda

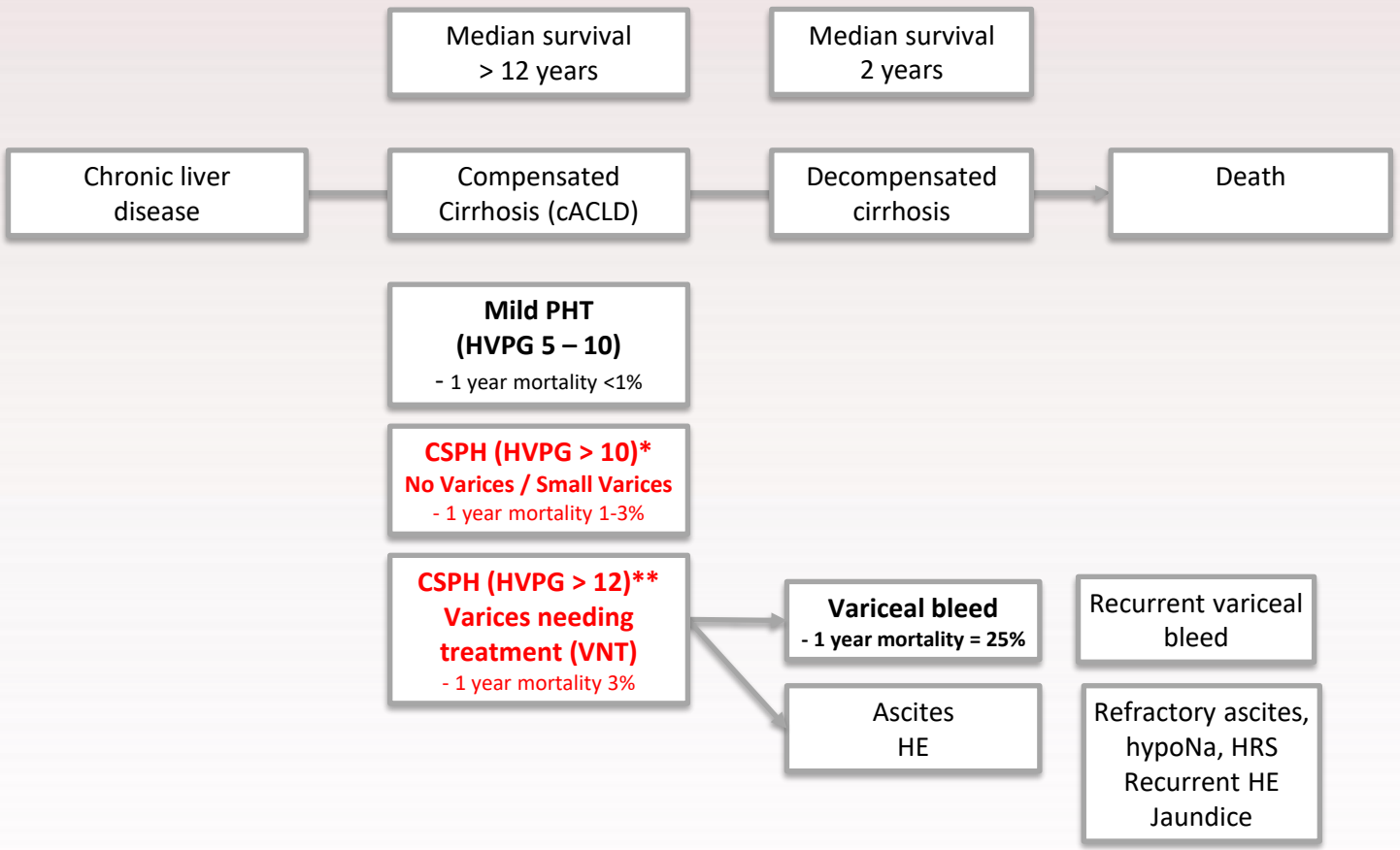
- Non-invasive tools to **rule in** clinically significant portal hypertension
  - **How?** - Liver stiffness measurement
  - **Why?** - non-selective B-blockers prevent first liver decompensation event

- Non-invasive tools to **rule out** oesophageal varices needing treatment
  - **How?** – LSM + platelet count

Recommendations for the assessment of metabolic dysfunction-associated fatty liver disease (MAFLD) in primary care: a consensus statement. GESA 2024

Non-invasive tools to rule in clinically significant portal hypertension (CSPH)

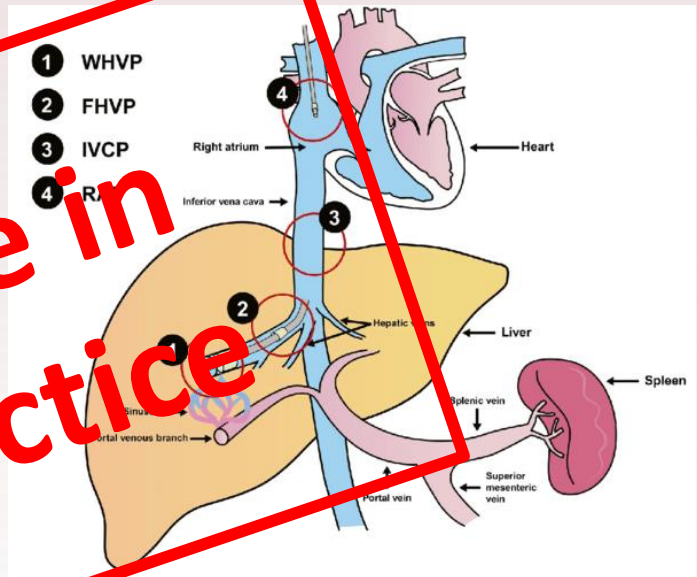
Clinically significant portal hypertension (CSPH)



HVPG (hepatic venous pressure gradient)

HVPG	
< 5	Normal
> 5	Sinusoidal PHT
> 10 (CSPH)	- Varices - Surgical risk (HCC)
> 12	- Variceal bleeding - Ascites - Encephalopathy
> 16	- Variceal bleeding - Ascites - Encephalopathy - SBP - HRS - Surgical risk (non-HCC abdominal surgery)

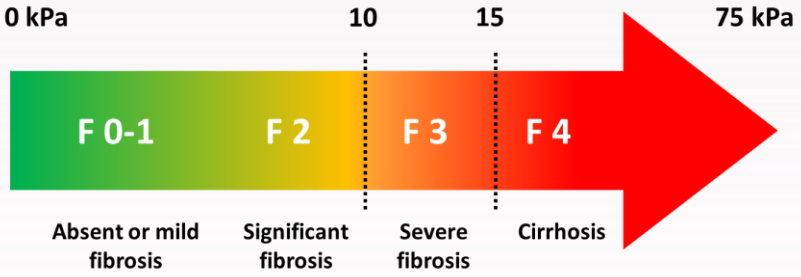
Rarely done in clinical practice



De Franchis R, Journal of Hepatology, 2022

Diagnosis of CSPH using Elastography

Liver Stiffness Measurement (LSM)
- elastography (e.g. Fibroscan™)

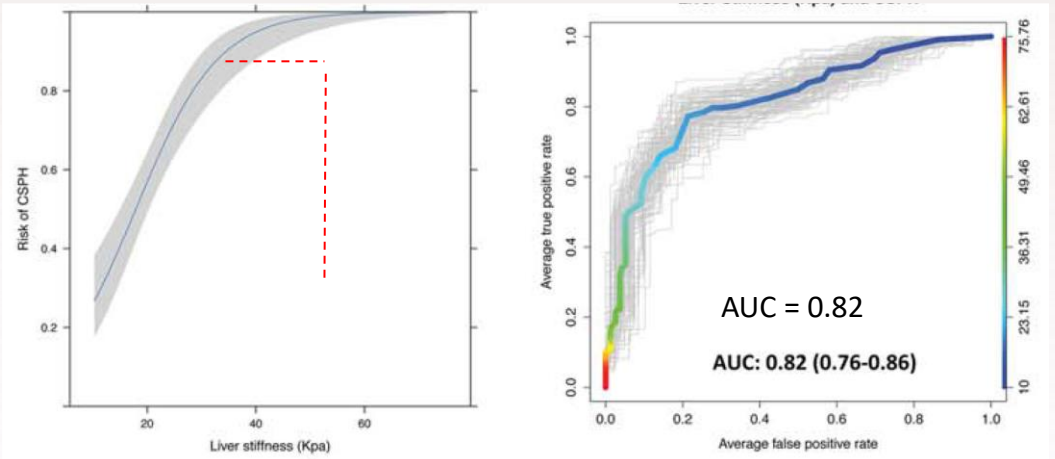


CSPH (PPV> 90%*,):**

"Anticipate trial":

LSM ≥ 25 kPa

n = 518



* Viral hepatitis, alcohol, non-obese MAFLD
** ANTICIPATE-NASH model for obese-MAFLD

Augustin, Hepatology, 2017

Diagnosis of CSPH using Elastography

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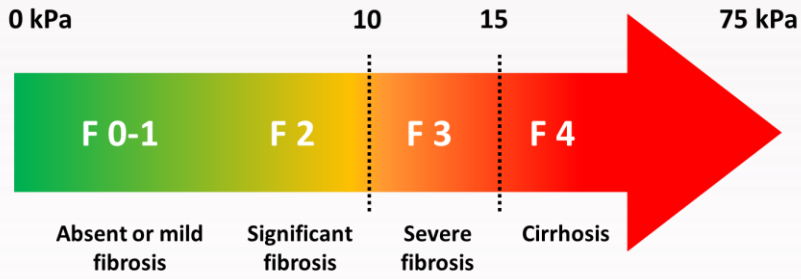


CSPH (PPV> 90%*,):**

"Anticipate trial":

LSM ≥ 25 kPa

LSM 20-25 kPa
+ Platelets 100 – 150

LSM 15-20 kPa
+ Platelets <110

* Viral hepatitis, alcohol, non-obese MAFLD
** ANTICIPATE-NASH model for obese-MAFLD

Augustin, Hepatology, 2017

CSPH - ARFI

Radiology

REVIEWS AND COMMENTARY • STATEMENTS AND GUIDELINES

Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement

Richard G. Barr, MD, PhD • Stephanie R. Wilson, MD • Deborah Rubens, MD • Guadalupe Garcia-Tsao, MD • Giovanna Ferraioli, MD

From the Department of Radiology, Northeastern Ohio Medical University, Rootstown, Ohio (R.G.B.); Department of Radiology, University of Calgary, Calgary, Canada (S.R.W.); Departments of Imaging Science, Oncology, and Biomedical Engineering, University of Rochester Medical Center, Rochester, NY (D.R.); Section of Digestive Diseases, Department of Medicine, Yale University, New Haven, Conn (G.G.T.); and Ultrasound Unit, Department of Clinical Sciences and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, University of Pavia, Pavia, Italy (G.F.). Received October 31, 2019; revision requested December 11; revision received April 2, 2020; accepted April 23. **Address correspondence to** R.G.B., Southwoods Imaging, 7623 Market St, Youngstown, OH 44512 (e-mail: *rgbarr525@gmail.com*).

Conflicts of interest are listed at the end of this article.

Radiology 2020; 296:263–274 • https://doi.org/10.1148/radiol.2020192437 • Content codes: GI US

- Thresholds have been defined for identifying CSPH
  - Less well validated than Fibroscan™

Table 2: Recommendation for Interpretation of Liver Stiffness Values Obtained with ARFI Techniques in Patients with Viral Hepatitis and NAFLD

Liver Stiffness Value	Recommendation
≤5 kPa (1.3 m/sec)	High probability of being normal
<9 kPa (1.7 m/sec)	In the absence of other known clinical signs, rules out cACLD. If there are known clinical signs, may need further test for confirmation
9–13 kPa (1.7–2.1 m/sec)	Suggestive of cACLD but need further test for confirmation
>13 kPa (2.1 m/sec)	Rules in cACLD
>17 kPa (2.4 m/sec)	Suggestive of CSPH

Note.—ARFI = acoustic radiation force impulse, cACLD = compensated advanced chronic liver disease, CSPH = clinically significant portal hypertension, NAFLD = non-alcoholic fatty liver disease.

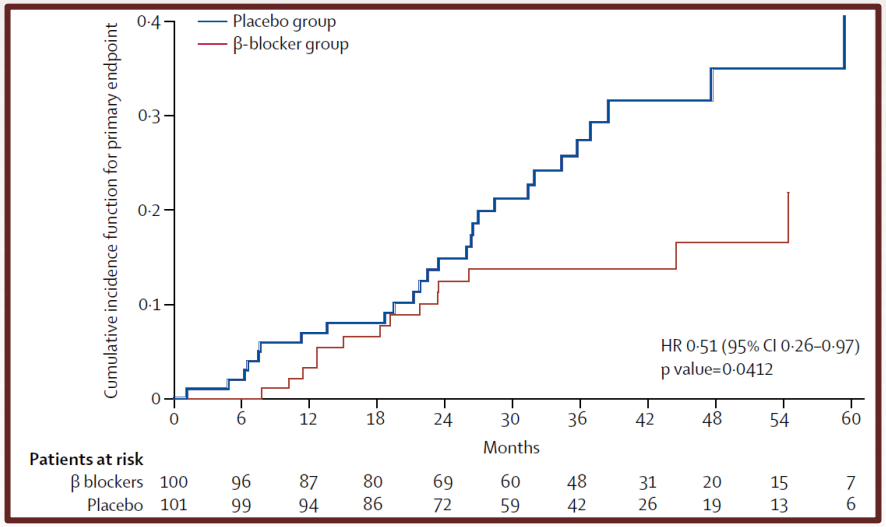
ARFI > 2.4m/s (17 kPa) = CSPH

Barr R, Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement, Radiology, 2020

Non-selective B-blockers improve outcomes in CSPH

PREDESCI study

- RCT evaluating the benefit of lowering HVPG with non-selective β blockers
- Inclusion criteria = HVPG ≥ 10 (n=201)
  - All patients were tested for reactivity to B-blocker (HVPG decrease > 10%)
    - Responders randomized to propranolol (up to 160mg BD) vs placebo
    - Non-responders were randomised to **carvedilol** (≤25mg daily) vs placebo
  - Primary endpoint - cirrhosis decompensation (ascites, bleeding, or HE) or death



Ascites
20% β blockers
9% placebo

NS-β blockers reduced the risk of first liver decompensation event (major effect - reducing the incidence of ascites)

Approach to Dx and Mx of CSPH in patients with compensated cirrhosis

- Liver stiffness measurement

↓

- CSPH – LSM ≥ 25 kPa (ARFI > 2.4 m/sec)

↓

- Start B-blocker to prevent decompensation
  - Carvedilol is the preferred NSBB
    - Note – these patients **do not need a gastroscopy** to screen for oesophageal varices needing treatment
      (NSBB = first-line primary prophylaxis for large varices in compensated cirrhosis)

What if you don't have access to liver stiffness measurement (elastography)?

- Diagnosis of CSPH:
  - Platelets < 110 - Y
  - Abdominal imaging - Y
    - porto-systemic shunts
  - Gastroscopy - Y
    - varices
  - Other NITs? – N
    - eg. FIB-4, ELF
    - Not yet validated for the diagnosis of CSPH

- Start carvedilol to prevent decompensation

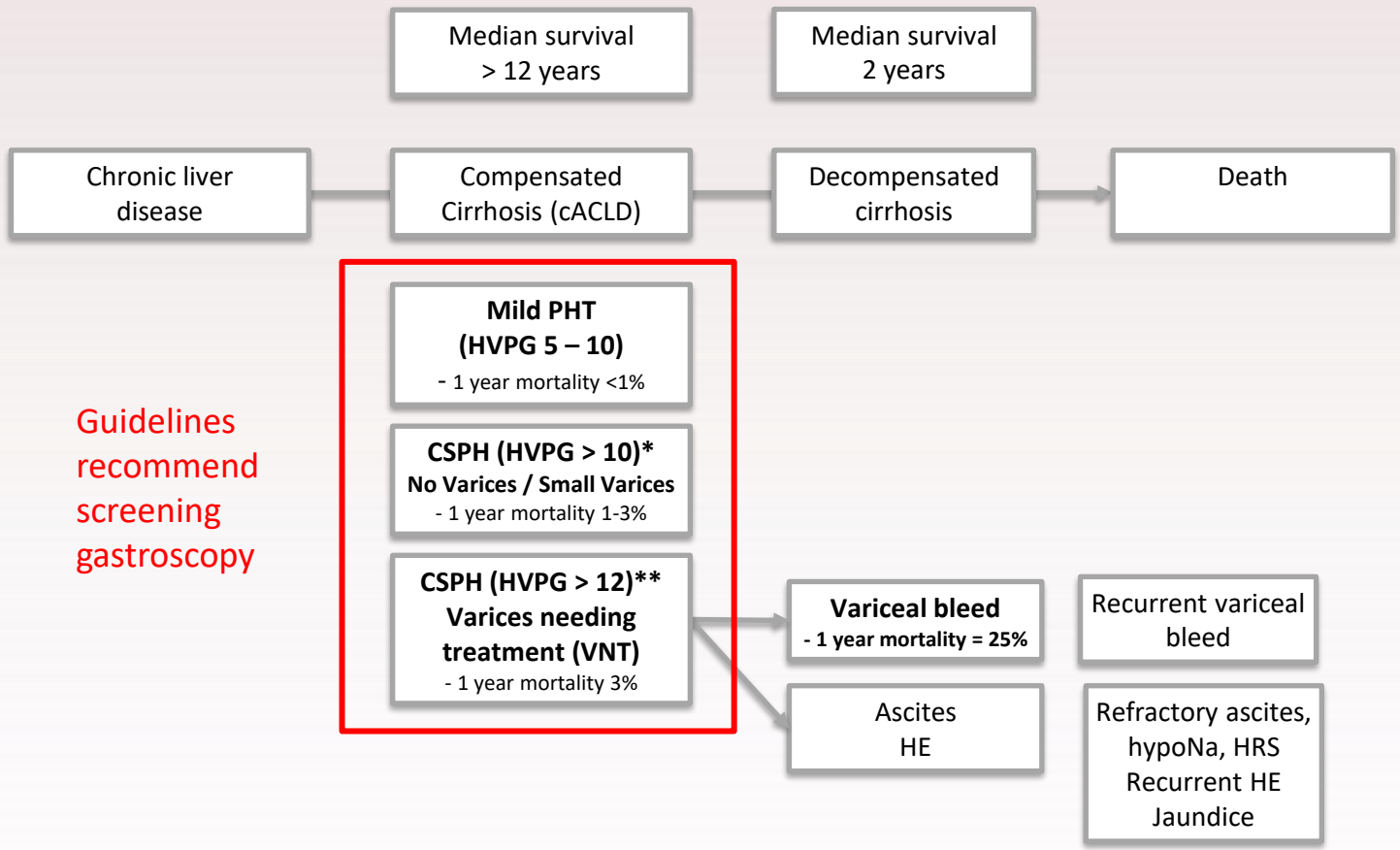
Clinically significant portal hypertension (CSPH)

- Dx of CSPH is important because it identifies patients with an increased risk of first liver decompensation event
- CSPH can be diagnosed non-invasively using elastography
  - Fibroscan – LSM > 25 kPa
  - ARFI – shear wave speed > 2.4 m/s
- NSBB (carvedilol) reduce the risk of first liver decompensation event in patients w CSPH

Recommendations for the assessment of metabolic dysfunction-associated fatty liver disease (MAFLD) in primary care: a consensus statement. GESA 2024

Non-invasive tools to rule out oesophageal varices needing treatment (VNT)

Clinically significant portal hypertension

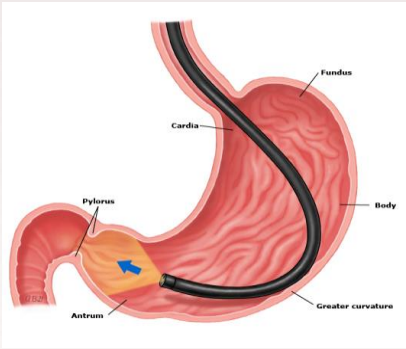


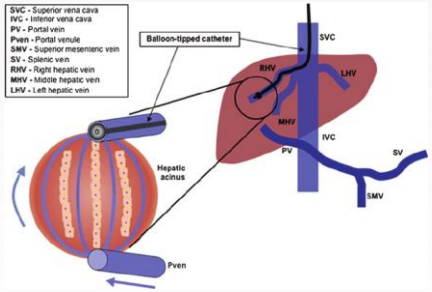
Screening presents a service challenge

Fibroscan,
Liver stiffness measurement (LSM)

Increasing numbers of people with compensated cirrhosis (cACLD)

Demand for gastroscopy for variceal screening
+++



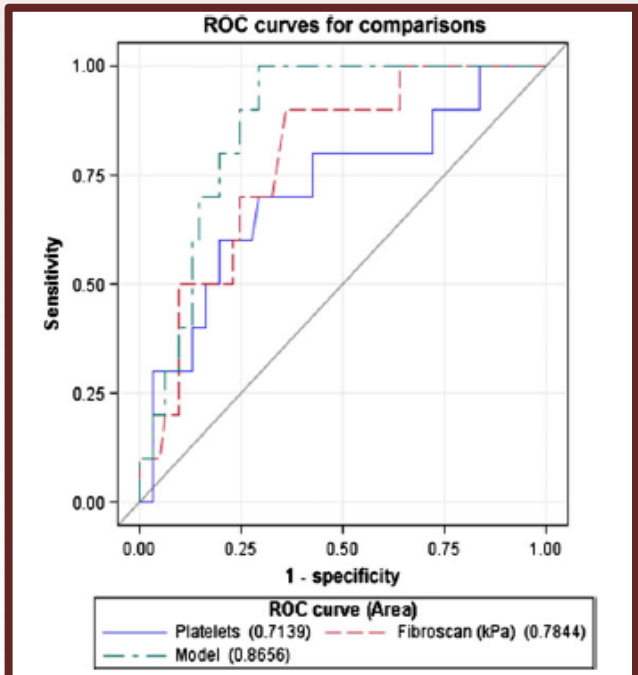


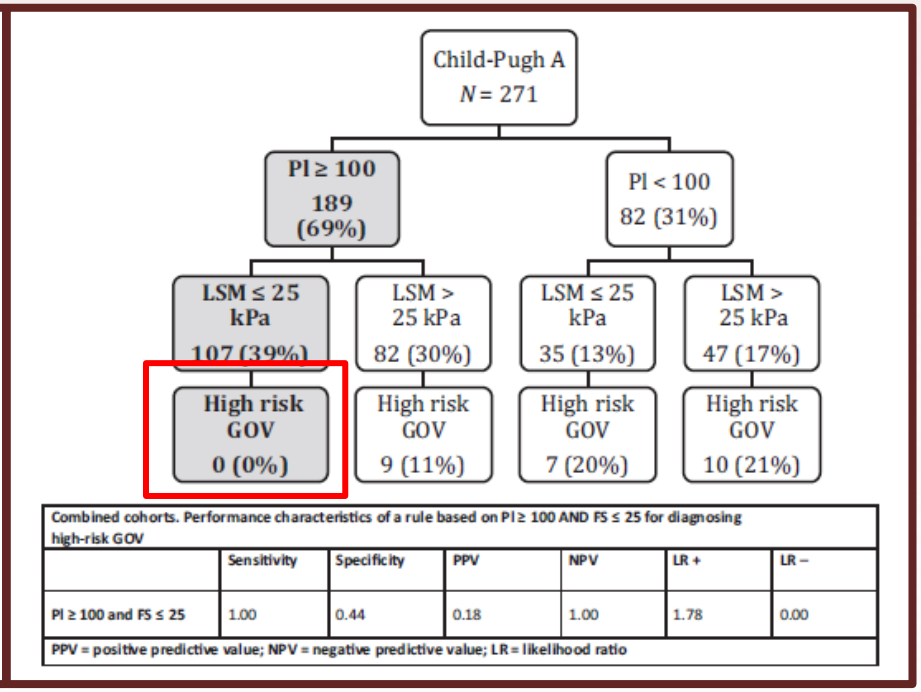
HVPG measurement not widely available
Capacity limited where available

Invasive
$$

LSM + platelets can be used to rule out VNT

Discovery cohort – n = 71
Validation cohort – n = 200, 2 independent centres





Combined cohorts. Performance characteristics of a rule based on PI ≥ 100 AND FS ≤ 25 for diagnosing high-risk GOV

	Sensitivity	Specificity	PPV	NPV	LR +	LR –
PI ≥ 100 and FS ≤ 25	1.00	0.44	0.18	1.00	1.78	0.00

PPV = positive predictive value; NPV = negative predictive value; LR = likelihood ratio

39% would avoid
screening gastroscopy

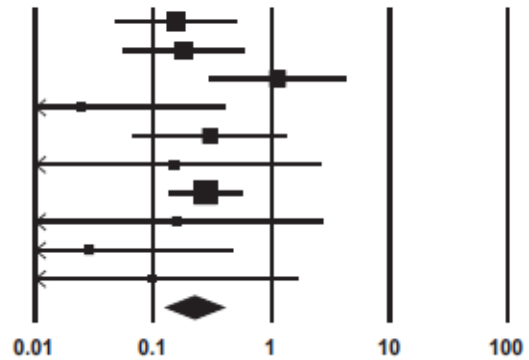
Ding N, Liver International, 2016

Baveno criteria to rule out VNT

- Baveno VI [1]
  - LSM < 20 kPa AND
  - platelet count > 150

→ **Spares 21% gastroscopy**
Miss rate for VNT < 5%

Study name	Subgroup within study	Statistics for each study					With varices/total	
		Odds ratio	Lower limit	Upper limit	Z-value	P-value	With low liver stifness and normal platelet count	With high liver stifness or low platelet count
Abraldes 2016	High risk varices	0.157	0.048	0.517	–3.048	.002	3/87	54/292
Ahmed 2016	High risk varices	0.180	0.055	0.590	–2.831	.005	3/111	49/367
Chang 2016	High risk varices	1.126	0.296	4.281	0.174	.862	3/34	11/139
Ding 2016	High risk varices	0.024	0.001	0.403	–2.593	.010	0/107	26/164
Maurice 2016	High risk varices	0.300	0.066	1.355	–1.565	.118	2/102	13/208
Paternostro 2016	High risk varices	0.150	0.008	2.682	–1.289	.197	0/10	19/80
Puigvehi 2016	High risk varices	0.278	0.135	0.572	–3.480	.001	10/149	45/219
Silva 2016	High risk varices	0.157	0.009	2.765	–1.265	.206	0/12	20/100
Thabut 2016	High risk varices	0.029	0.002	0.468	–2.493	.013	0/156	49/493
Tosetti 2016	High risk varices	0.097	0.006	1.673	–1.606	.108	0/39	12/107
Pool estimate risk		0.224	0.128	0.391	–5.241	.000		



In patients with low LSM and normal platelets , the pooled estimate rates for VNT was 0.040 (95% CI = 0.027 – 0.059) [2]

1 – De Franchis R, J Hepatology, 2015
2 – Marot A, Liver Int, 2017

Baveno criteria to rule out VNT

- Baveno VI [1]
  - LSM < 20 kPa AND
  - Platelet count > 150

→ **Spares 21% gastroscopy**
Miss rate for VNT < 5%

- Expanded Baveno (VII) [2]
  - LSM < **25** kPa AND
  - Platelet count > **110**

→ **Spares 40% gastroscopy**
Miss rate for VNT < 5%

➢ More recently validated for NASH cirrhosis using the XL probe [3] and MAFLD cirrhosis [4]

1 – De Franchis R, J Hepatology, 2015
2 – Augustin S, Hepatology, 2017
3 – Petta S, J Hepatology, 2018
4 – Qi X, J Hepatology, 2020

Who still needs a gastroscopy to screen for varices needing treatment (1^0 prophylaxis)?

- Patients w CSPH taking carvedilol 
- Patients w CSPH intolerant of carvedilol 
- Patients with LSM < 20 kPa AND Pl > 150 
- Patients with LSM > 20 kPa OR Pl < 150 

In patients with compensated cirrhosis

- TREAT THE LIVER DISEASE
- CSPH identifies an increased risk of first liver decompensation event
- CSPH can be diagnosed non-invasively
  - Fibroscan (**LSM > 25 kPa**)
  - ARFI (shear wave speed > 2.4m/s)
- Patients with CSPH should be treated w **carvedilol** to reduce the risk of first liver decompensation event
  - Screening gastroscopy for VNT is not indicated
- Screening gastroscopy for VNT should be reserved for:
  - Patients with CSPH who are intolerant of carvedilol
  - Patients with LSM > 20 kPa **OR** Pl < 150

What else is new in portal HT

- Albumin infusions for resistant ascites
  - Weekly albumin

- Pre-emptive TIPS < 72 hours after acute variceal bleed for patients at high risk of re-bleeding
  - CP-B8-9 w active bleeding at endoscopy
  - CP-C10-13

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Guidance documents coming in 2024

- Diagnosis and Management of Portal Hypertension in Advanced Liver Disease: An Australian Consensus Statement

- An Australian Consensus Statement on the role of TIPS in the management of portal hypertension