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Metabolic Dysfunction associated Fatty Liver Disease (MAFLD) Case Presentation

Dr Chuah Kee Huat
University of Malaya



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Acknowledgement

- The two cases used in this presentation are courtesy of Professor Dr Chan Wah Kheong.

Case 1

- 48 years old gentleman
- DM, Dyslipidemia, Hypothyroidism
- On Vildagliptin 50 mg/Metformin 500 mg twice daily, Repaglinide 2 mg three times daily, Simvastatin 5 mg at night, L-thyroxine 200 mcg daily
- Referred for persistently deranged liver profile and fatty liver on ultrasonography
- Alcohol intake during occasions only in small amounts
- No other medications

Case 1

- BP 110/80 mmHg
- Physical examination unremarkable
- Weight 85.5 kg, Height 1.69 m, BMI 29.9 kg per m²
- Hb 13.8 g/dl, WBC 5.2 x 10⁹/L, Platelet 168 x 10⁹/L
- Albumin 36 g/L, Bilirubin 12 μmol/L, ALT 118 U/l, AST 87 U/L, GGT 158 U/L, INR 1.1
- Creatinine 78 mmol/L
- HbA1c 7.3%, TG 1.9 mmol/L, LDL 2.8 mmol/L
- HBsAg not detected, anti-HCV not detected

MAFLD/ NAFLD – Assessment

Assessment	Result	Action	
Blood tests (e.g. ALT and AST)	Normal ALT and AST	Repeat ALT and AST annually	
	Elevated ALT and AST*	<ul style="list-style-type: none"> - US abdomen to diagnose fatty liver/exclude focal liver lesion - Repeat ALT and AST after 3-6 months 	<ul style="list-style-type: none"> - Exclude other causes of liver disease - Consider referral to Gastroenterologist / Hepatologist

* Exclude possibility of drug-induced liver injury.

ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; US: ultrasound.

NAFLD – Assessment

Assessment	Result	Action
Fibrosis-4 scoring	Fibrosis-4 index <1.3	Repeat every 2-3 years
	Fibrosis-4 index ≥1.3	Refer for liver stiffness measurement Consider referral to Gastroenterologist / Hepatologist

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST (U/L)}}{\text{Platelet count (x } 10^9/\text{L)} \times \text{ALT (U/L)}^{1/2}}$$

FIB-4	Interpretation
<1.3	Low risk for advanced fibrosis
≥ 1.3	Intermediate to high risk for advanced fibrosis

Fibrosis-4 (FIB-4) Calculator

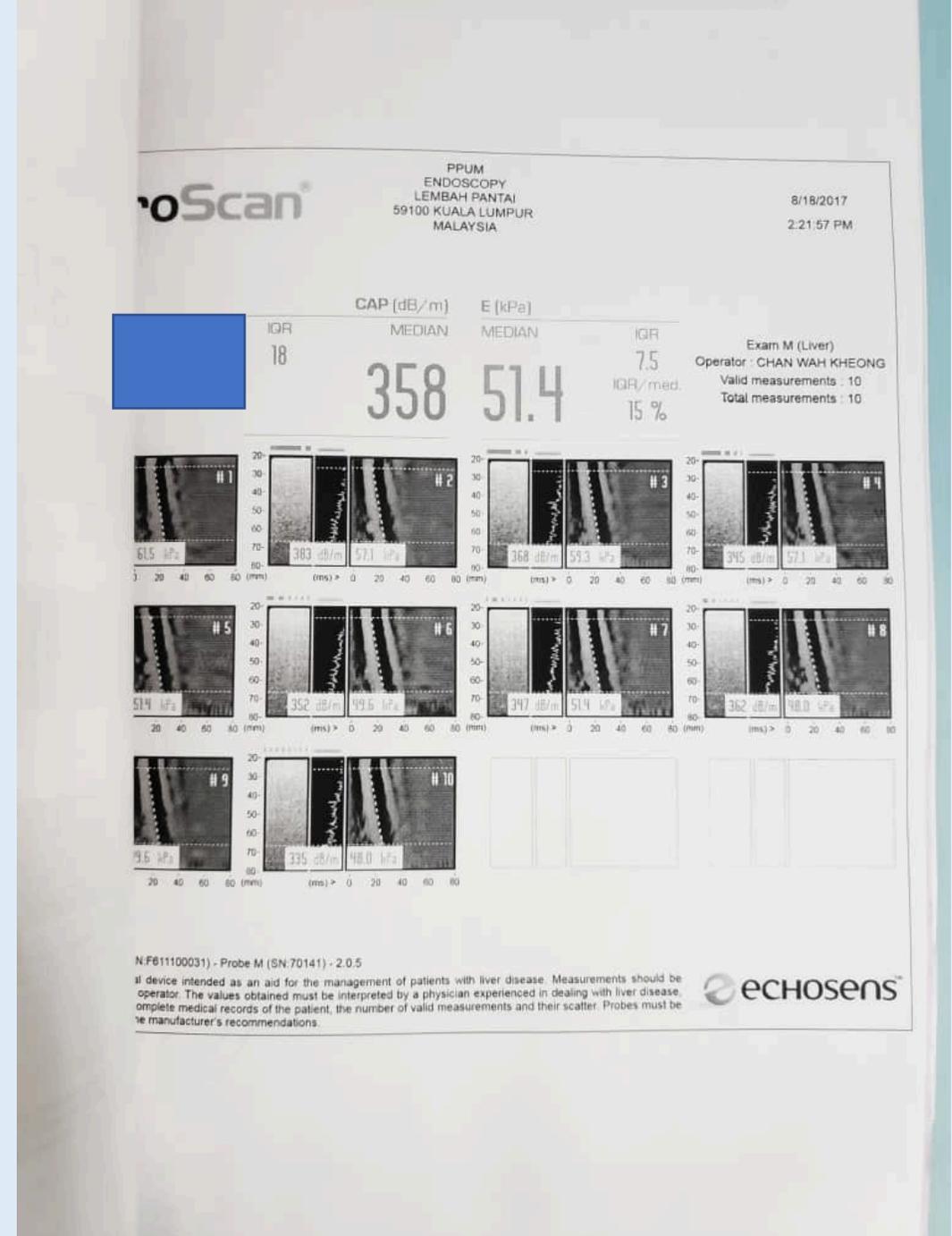
Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = 2.29$$

Fibroscan (18/8/2017)

- Valid measurements: 10
- Total measurements: 10
- IQR/median: 15%
- LSM: 51.4 kPa
- CAP: 358 dB/m



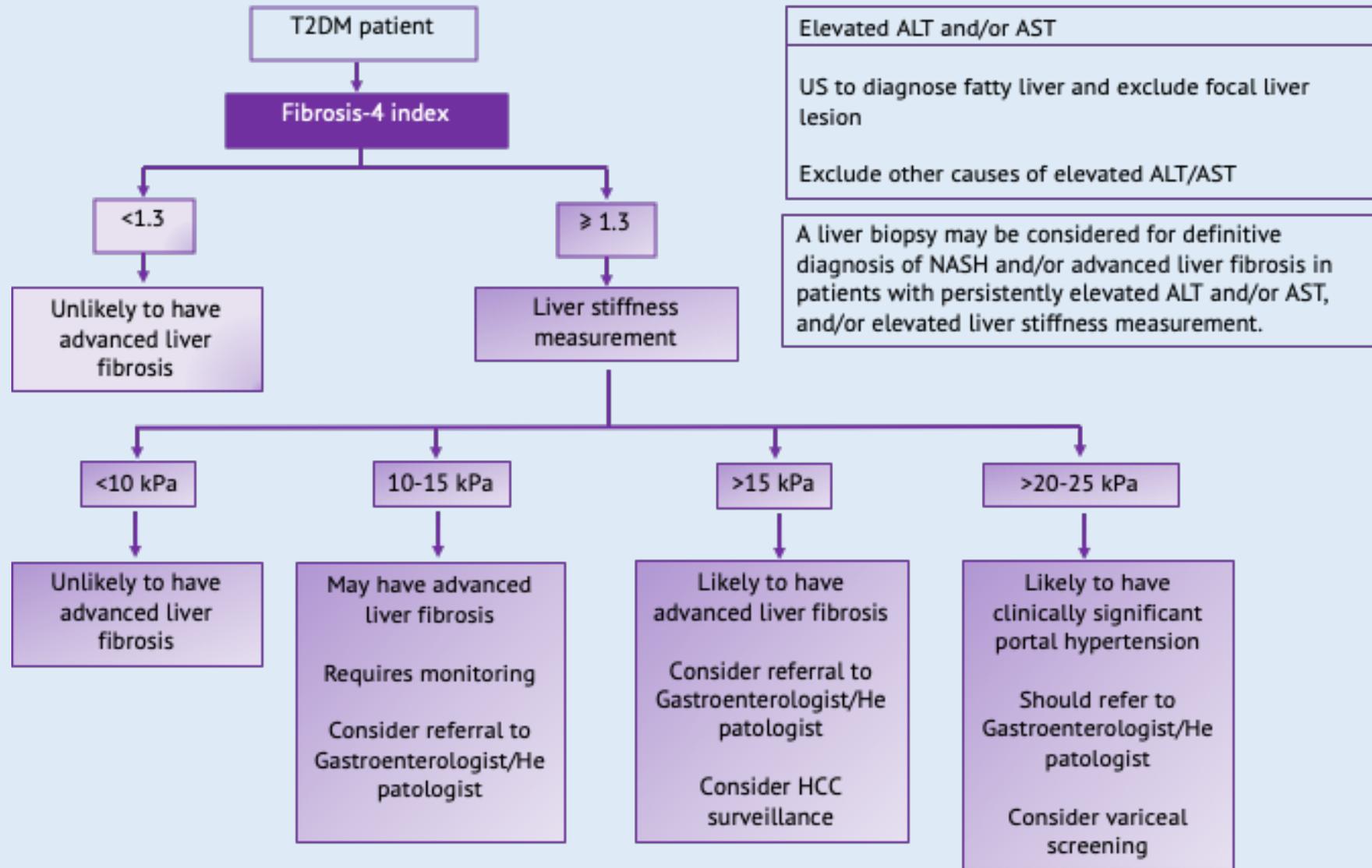
Liver stiffness measurement

Liver stiffness (kPa)*	Interpretation	Action
< 10	Unlikely to have advanced fibrosis	
10-15	May have advanced liver fibrosis	<ul style="list-style-type: none"> • Requires monitoring e.g. repeat in 1 year • Consider referring to Gastroenterologist / Hepatologist
> 15	Likely to have advanced liver fibrosis	<ul style="list-style-type: none"> • Should be considered for HCC surveillance • Consider referring to Gastroenterologist / Hepatologist
> 20-25 (+/- presence of thrombocytopenia)	Likely to have clinically significant portal hypertension	<ul style="list-style-type: none"> • Should be considered for HCC surveillance and variceal screening • Requires referral to Gastroenterologist / Hepatologist

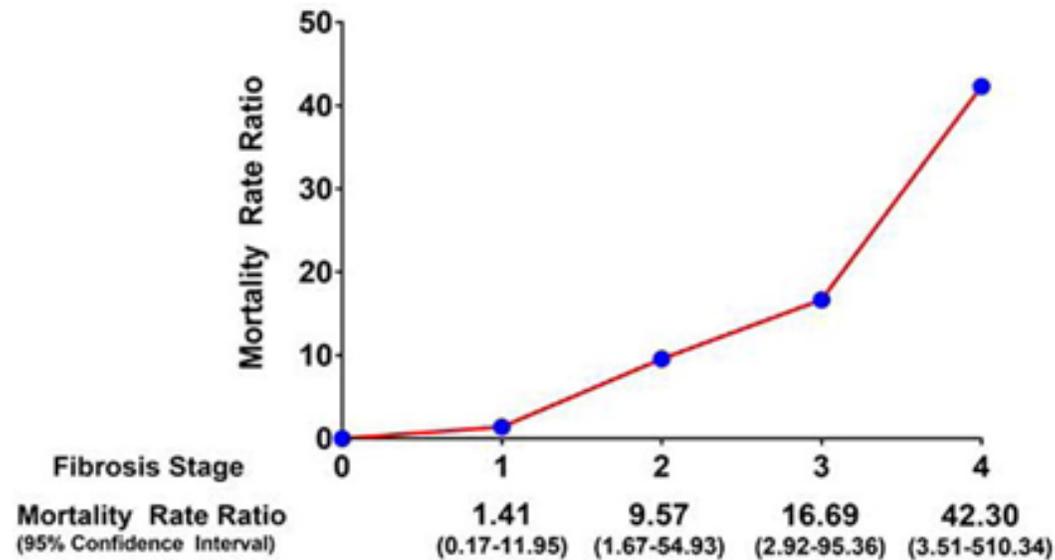
*Values obtained by transient elastography. kPa: kilopascals; HCC: hepatocellular carcinoma.
Adapted from Wong VW, et al. *Gut*. 2019;68(11):2057-2064.

References: 1. CPG Management of Type 2 Diabetes Mellitus (6th Edition)

Assessment of NAFLD in patients with T2DM



Fibrosis stage is the single most important predictor of liver related mortality

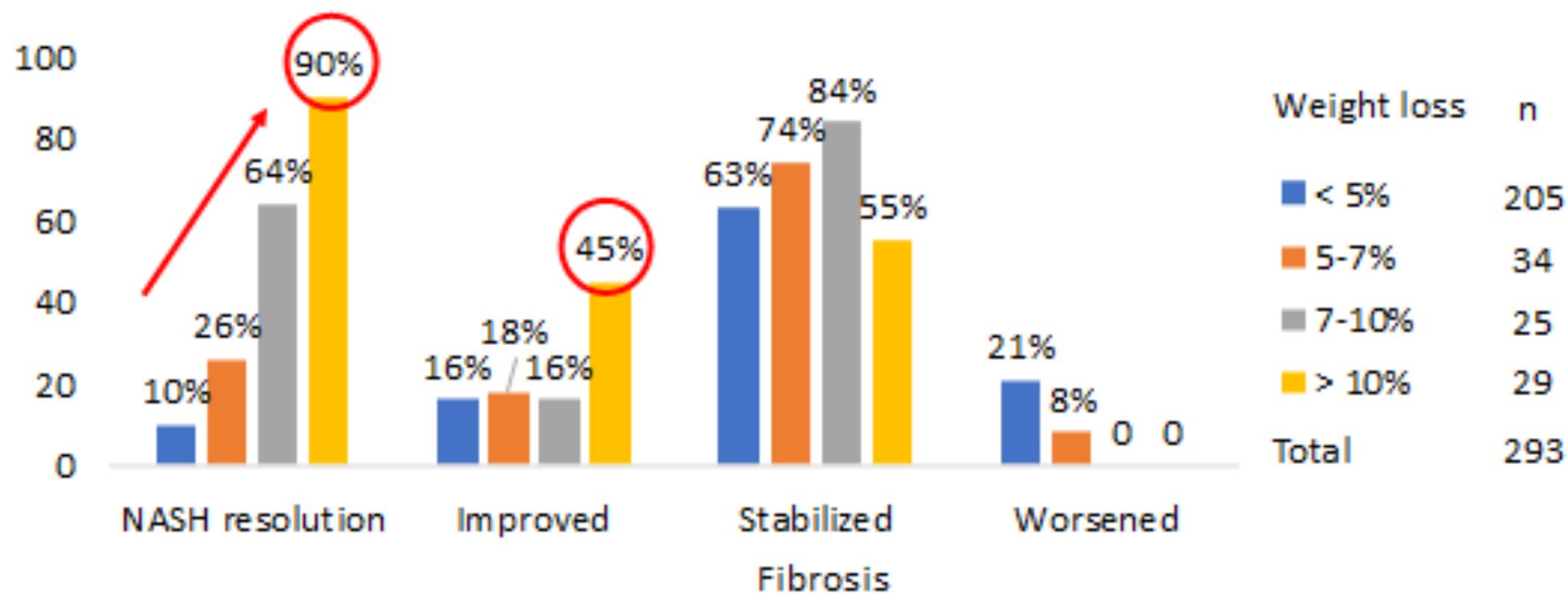


Dulai *et al*, *Hepatology* 2017

Case 1

- Given advice on diet, exercise and weight loss $\geq 10\%$
- Stopped repaglinide
- Empagliflozin 25mg daily
- Silymarin 140 mg three times daily

Lifestyle intervention in NAFLD



Vilar-Gomez E, et al. Gastroenterology 2015.

RCT of silymarin for the treatment of biopsy-proven NASH

- Higher proportion of patients in the silymarin group had fibrosis improvement (22.4%) compared with the placebo group (6.0%; $p=0.023$).

Chan WK, et al. Clin Gastroenterol Hepatol 2017

Single arm study of empagliflozin for the treatment of biopsy-proven NASH

- Empagliflozin resulted in significantly greater improvements in steatosis (67% vs. 26%, $p=0.025$), ballooning (78% vs. 34%, $p=0.024$), and fibrosis (44% vs. 6%, $p=0.008$) compared with historical placebo.

Lai LL, et al. Dig Dis Sci 2019

OGDS for variceal screening



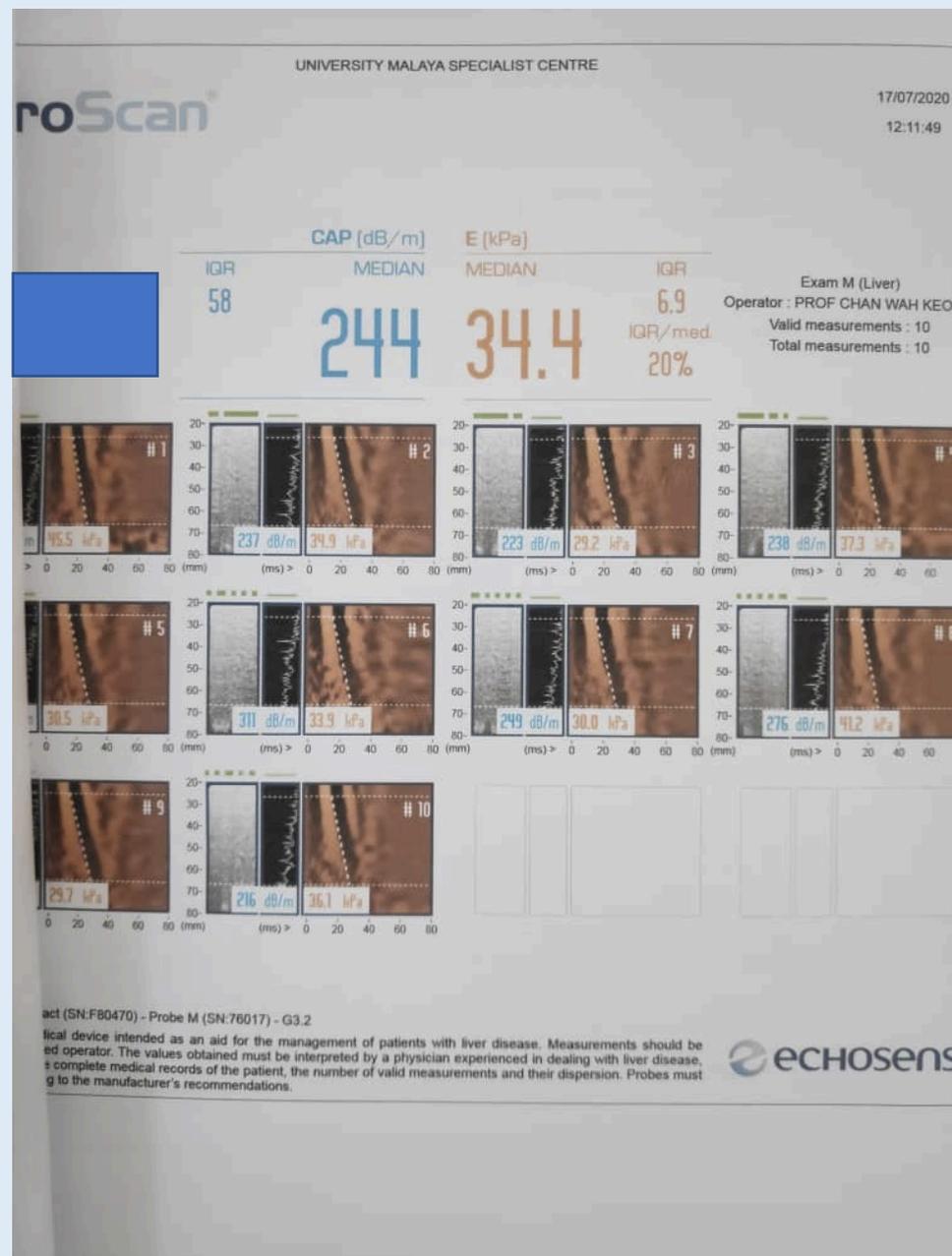
- Large esophageal varices with red wale marking and portal hypertensive gastropathy
- Endoscopic variceal ligation performed and started on propranolol

Follow-up

- After 1 month
- Weight 82 kg (baseline 85.5 kg; TBWL 4.1%)
- Liver profile improved, HbA1c 6.9, lipid profile normalized

Fibroscan (17/7/2020)

- Valid measurements: 10
- Total measurements: 10
- IQR/median: 20%
- LSM: 34.4 kPa
- CAP: 244 dB/m



Repeat OGDS after 6 months



- Small esophageal varices with scarring from previous endoscopic treatment

Follow-up

- HCC surveillance with US and AFP 6-monthly
- After 8 months
- Weight 74.5 kg (baseline 85.5 kg; TBWL 12.9%)
- Liver profile normalized, HbA1c 6.5, lipid profile normalized



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Case 2

- 53 years old Chinese lady
- Dyslipidemia on simvastatin 20 mg at night
- No alcohol or traditional medication
- Referred for abnormalities in liver profile

Case 2

- BMI 28 kg/m²
- BP 140/88 mmHg
- Albumin 40 g/L, Bilirubin 7 μmol/L, ALP 115 U/L, ALT 140 U/L, AST 80 U/L, GGT 98 U/L
- Platelet 286 x 10⁹/L
- Other blood results:
 - TG 0.9 mmol/L, TC 4.4 mmol/L, HDL 1.33mmol/L, LDL 2.66 mmol/L
 - FBS 5.9 mmol/L, HbA1c 5.4 %
 - HBs Ag negative, anti-HCV negative
- US showed fatty liver

Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count (10}^9\text{/L)} \times \sqrt{\text{ALT (U/L)}}} = 1.25$$

The calculation uses the following values:

- Age (years): 53
- AST Level (U/L): 80
- Platelet Count (10⁹/L): 286
- ALT (U/L): 140

Follow-up

- After 6 months of lifestyle intervention, her weight remained the same
- ALT 111 U/L, AST 62 U/L, GGT 77 U/L
- Liver biopsy 
- Started on vitamin E 800 IU/day
- After 6 months, her weight remained the same
- ALT 42 U/L, AST 39 U/L, GGT 45 U/L

Histology

Steatosis

0

1

2

3

Inflammation

0

1

2

3

Ballooning

0

1

2

Fibrosis

0

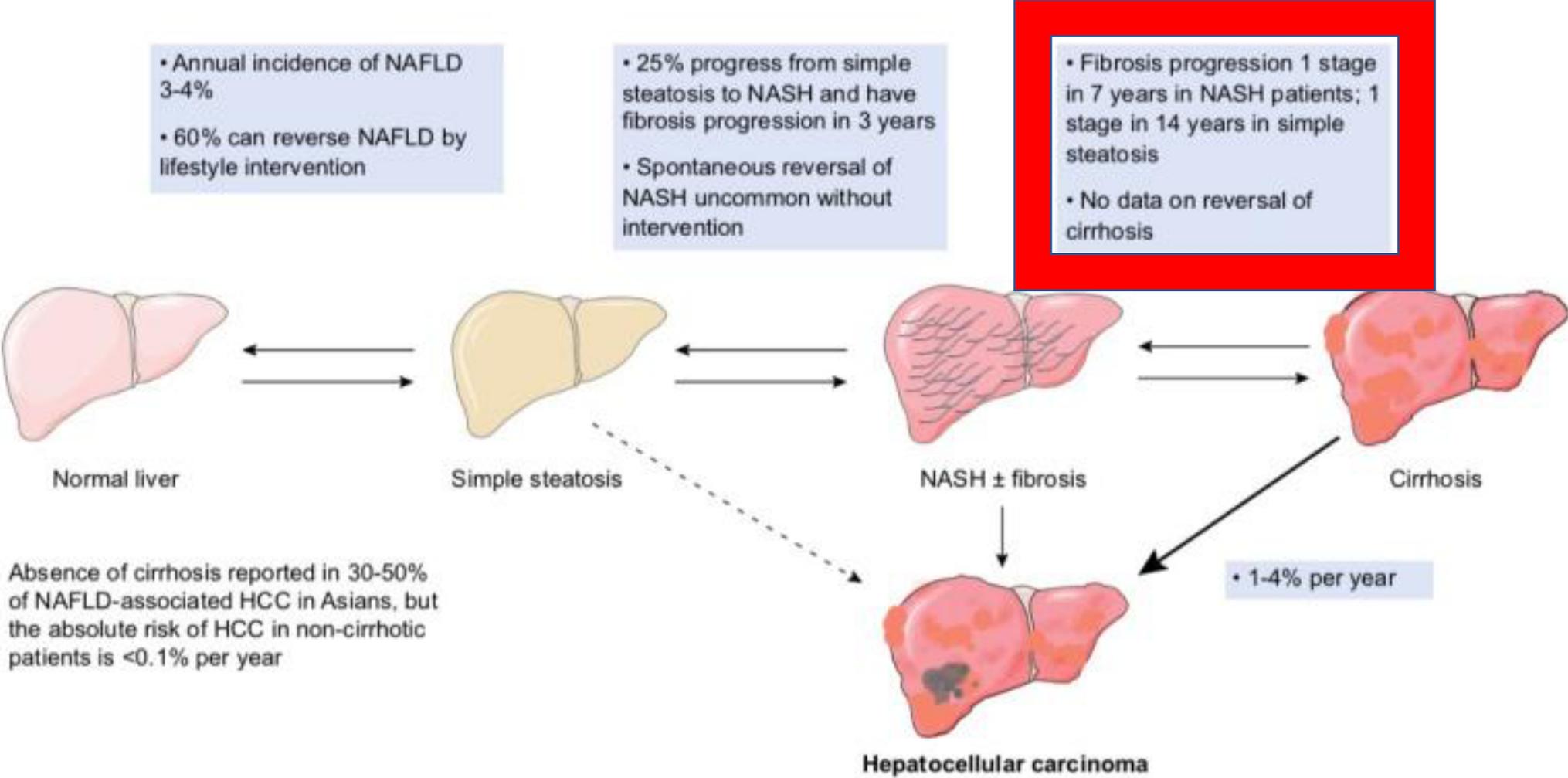
1

2

3

4

Natural history of NAFLD



- Thank you

