Assessment and Management of NAFLD/NASH

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Non-alcoholic fatty liver disease (NAFLD)

- Excess accumulation of fat in the liver
- Related to over-nutrition
- For a strict definition of NAFLD, significant (or excessive) alcohol consumption and other causes of chronic liver disease must be excluded

Healthy liver  
Fatty liver

Wong VW, Chan WK et al, J Gastroenterol Hepatol 2017
NAFLD: the liver manifestation of metabolic syndrome
Non-alcoholic steatohepatitis (NASH)

- The more severe form of NAFLD, characterized by lobular inflammation and hepatocyte ballooning
- Can lead to fibrosis and cirrhosis
Stages of fibrosis in NAFLD


- **F0**: No fibrosis
- **F1**: Perisinusoidal fibrosis
- **F2**: Perisinusoidal with portal/periportal fibrosis
- **F3**: Bridging fibrosis
- **F4**: Cirrhosis

**Advanced fibrosis**
Spectrum of NAFLD

Simple steatosis | NASH +/- advanced fibrosis | Cirrhosis

Cardiovascular disease

Hepatocellular carcinoma

Hepatic decompensation

Musso et al, Ann Med 2011
White et al, Clin Gastroenterol Hepatol 2012
Cascade of interventions

Treatment for metabolic syndrome

Lifestyle intervention ± pharmacological therapy
Bariatric procedure for select patients

Anti-inflammatory

Anti-fibrotic

Simple steatosis  NASH +/- advanced fibrosis  Cirrhosis
Simple steatosis

Prevalence of NAFLD ~ 20% – 30%
6 million – 9 million

Prevalence of NASH 2% – 3%
600,000 – 900,000

Non-alcoholic steatohepatitis (NASH)

Fibrosis/Cirrhosis
Risk of decompensated liver disease and HCC

Malaysian population
30 million

F0 29.3%
F1 41.5%
F2 8.2%
F3 19.0%
F4 2.0%

Prevalence of advanced fibrosis among NASH patients ~ 20%
120,000 – 180,000

Serum AST level for the diagnosis of NASH

<table>
<thead>
<tr>
<th>AST Level</th>
<th>Non-NASH</th>
<th>NASH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 37 IU/L</td>
<td>6</td>
<td>35</td>
<td>41</td>
</tr>
<tr>
<td>≥ 37 IU/L</td>
<td>4</td>
<td>48</td>
<td>52</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>83</td>
<td>93</td>
</tr>
</tbody>
</table>

Upper limit of normal for serum AST level = 37 IU/L

Diagnosis of NASH based on pathologist global assessment

- Elevated serum AST level in NAFLD patients is strongly suggestive of NASH
- Normal serum AST level has poor predictive value for the absence of NASH

## Asia-Pacific NASH Risk Score

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>&lt; 30 kg/m²</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥ 30 kg/m²</td>
<td>2</td>
</tr>
<tr>
<td>DM</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>ALT</td>
<td>&lt; 88 U/L</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥ 88 U/L</td>
<td>1</td>
</tr>
<tr>
<td>AST</td>
<td>&lt; 38 U/L</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥ 38 U/L</td>
<td>1</td>
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</tbody>
</table>

### Risk group

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Patients with NASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0-1)</td>
<td>32 – 39%</td>
</tr>
<tr>
<td>Moderate (2-3)</td>
<td>60 – 67%</td>
</tr>
<tr>
<td>High (4-6)</td>
<td>80 – 83%</td>
</tr>
</tbody>
</table>

Based on 1008 biopsy-proven NAFLD patients

Asia-Pacific NAFLD advanced fibrosis risk score

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt; 55 years</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥ 55 years</td>
<td>2</td>
</tr>
<tr>
<td>DM</td>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Platelet</td>
<td>≥ 150 x $10^9$/L</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>&lt; 150 x $10^9$/L</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Patients with advanced fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0)</td>
<td>4 – 5%</td>
</tr>
<tr>
<td>Moderate (1-2)</td>
<td>14 – 17%</td>
</tr>
<tr>
<td>High (3-4)</td>
<td>38 – 39%</td>
</tr>
</tbody>
</table>

Based on 1008 biopsy-proven NAFLD patients

The NAFLD fibrosis score for the prediction of advanced fibrosis

- AUROC 0.85
- However, 20 – 58 % will fall in the indeterminate group

< – 1.455: absence of advanced fibrosis
> 0.675: presence of advanced fibrosis
Between – 1.455 and 0.675: indeterminate

Transient elastography (Fibroscan)

- Different tissue has different stiffness
- Shear wave travels at different velocity in tissue with different stiffness
- Ultrasound is used to measure propagation of shear wave generated by an external vibrator
Transient elastography (Fibroscan)

- $V_S = 1.1 \text{ m/s}$
  - $E \sim 3 \text{ kPa}$

- $V_S = 1.7 \text{ m/s}$
  - $E \sim 9 \text{ kPa}$

- $V_S = 3.6 \text{ m/s}$
  - $E \sim 40 \text{ kPa}$

2.5 kPa  Without Fibrosis  Significant Fibrosis  Cirrhosis  75 kPa
Transient elastography (Fibroscan)

- Data for 101 patients were analyzed
- F0, 30.7%; F1, 44.6%; F2, 5.9%; F3, 15.8%; F4, 3.0%

<table>
<thead>
<tr>
<th></th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal cut-off, kPa</td>
<td>5.60</td>
<td>6.65</td>
<td>8.00</td>
<td>17.0</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>89.4</td>
<td>100.0</td>
<td>95.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>81.4</td>
<td>70.0</td>
<td>80.2</td>
<td>96.2</td>
</tr>
</tbody>
</table>

*Using optimal cut-off by Yoneda et al

Chan WK et al. Hepatol Int, 2015
Fibroscan for prediction of advanced fibrosis

AUROC 0.94


AUROC 0.93

Transient elastography (Fibroscan)
Stages of fibrosis in NAFLD

- **F0**: No fibrosis
- **F1**: Perisinusoidal fibrosis
- **F2**: Perisinusoidal with portal/periportal fibrosis
- **F3**: Bridging fibrosis
- **F4**: Cirrhosis

**Advanced fibrosis**

- Compensated
- Decompensated

Compensated advanced chronic liver disease (cACLD)

- The spectrum of severe fibrosis and cirrhosis is a continuum in asymptomatic patients, and distinguishing between the two is often not possible on clinical grounds.

Advanced fibrosis

F3: Bridging fibrosis

F4: Cirrhosis

Compensated

Decompensated

Criteria to suspect cACLD

- <10 kPa in the absence of other known clinical signs → rule out cACLD
- 10 – 15 kPa → suggestive of cACLD
- >15 kPa → highly suggestive of cACLD

Criteria to confirm cACLD

- Liver biopsy showing severe fibrosis or established cirrhosis
- Upper GI endoscopy showing gastroesophageal varices
- Hepatic venous pressure gradient (HVPG) measurement; values >5 mmHg indicate sinusoidal portal hypertension

Liver biopsy in NAFLD/NASH

- Disadvantages:
  - Expensive
  - Invasive
    - Small risk of complications
    - Not suitable for repeated assessments
  - Technical expertise required
  - Observer variability
  - Sampling variability
Lifestyle intervention

Vilar-Gomez et al, Gastroenterology 2015
Pioglitazone, vitamin E or placebo for NASH (PIVEN)

- Multicentre, randomized, double-blinded, placebo-controlled trial
- Biopsy-proven NASH without diabetes mellitus
- Vitamin E 800 IU daily vs. pioglitazone 30 mg daily vs. placebo for 96 weeks
- Primary efficacy outcome
  - Improvement in hepatocyte ballooning by ≥1 point
  - No increase in fibrosis
  - Decrease in NAFLD activity score (NAS) ≥2 points with ≥1 point decrease in steatosis or lobular inflammation

Sanyal et al, N Engl J Med 2010
Vitamin E

- Primary efficacy outcome: p = 0.001
- Steatosis: p = 0.005
- Lobular inflammation: p = 0.02
- Hepatocyte ballooning: p = 0.01
- Fibrosis: p = 0.24

- Conflicting reports of increased all cause mortality
- Prostate cancer

Sanyal et al, N Engl J Med 2010
Pioglitazone

- Primary efficacy outcome
  - Pioglitazone: 34%
  - Placebo: [VALUE]%
  - p = 0.04

- Steatosis
  - Pioglitazone: [VALUE]%
  - Placebo: [VALUE]%
  - p < 0.001

- Lobular inflammation
  - Pioglitazone: [VALUE]%
  - Placebo: [VALUE]%
  - p = 0.004

- Hepatocyte ballooning
  - Pioglitazone: [VALUE]%
  - Placebo: [VALUE]%
  - p = 0.08

- Fibrosis
  - Pioglitazone: [VALUE]%
  - Placebo: [VALUE]%
  - p = 0.12

- Weight gain
- Congestive cardiac failure
- Bladder cancer
- Osteoporosis

Sanyal et al, N Engl J Med 2010
Liraglutide

- Glucagon-like peptide-1 (GLP-1) receptor agonist
- Adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus

1. Delays gastric emptying
2. Increase insulin secretion
3. Decrease hepatic gluconeogenesis by decreasing glucagon secretion

Baggio et al, Gastroenterology 2007
Liraglutide safety and efficacy in patients with NASH (LEAN)

- Multicentre, randomized, double-blinded, placebo-controlled trial
- Overweight (BMI ≥ 25 kg per m^2) and biopsy-proven NASH
- Liraglutide 1.8 mg daily vs. placebo for 48 weeks
- Primary efficacy outcome: resolution of definite NASH (disappearance of hepatocyte ballooning) with no worsening in fibrosis
- Percentage of patients with diabetes mellitus: 33%
- Percentage of patients with fibrosis stage F3, 40%; F4, 12%

Armstrong et al, Lancet 2016
Liraglutide safety and efficacy in patients with NASH (LEAN)

Resolution of definite NASH

- Liraglutide: 9/23 (% = 39)
- Placebo: 2/22 (% = 9)

Progression of fibrosis

- Liraglutide: 8/22 (% = 36)
- Placebo: 2/23 (% = 9)

Significance:
- Resolution of definite NASH: p = 0.019
- Progression of fibrosis: p = 0.040

Armstrong et al, Lancet 2016
## Liraglutide safety and efficacy in patients with NASH (LEAN)

<table>
<thead>
<tr>
<th></th>
<th>Liraglutide, n = 23</th>
<th>Placebo, n = 22</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steatosis improvement</td>
<td>83%</td>
<td>45%</td>
<td>0.009</td>
</tr>
<tr>
<td>Lobular inflammation improvement</td>
<td>48%</td>
<td>55%</td>
<td>0.650</td>
</tr>
<tr>
<td>Hepatocyte ballooning improvement</td>
<td>61%</td>
<td>32%</td>
<td>0.050</td>
</tr>
<tr>
<td>NAS improvement</td>
<td>74%</td>
<td>64%</td>
<td>0.460</td>
</tr>
<tr>
<td>Fibrosis improvement</td>
<td>26%</td>
<td>14%</td>
<td>0.460</td>
</tr>
</tbody>
</table>

Armstrong et al, Lancet 2016
Liraglutide safety and efficacy in patients with NASH (LEAN)

- Similar adverse event profile to placebo, with the exception of predictable gastrointestinal symptoms (mainly diarrhoea, constipation, and loss of appetite), which were mainly transient and mild-to-moderate in severity.

Armstrong et al, Lancet 2016
Silymarin, derived from the milk thistle plant, *Silybum marianum*, has been used for centuries as a herbal remedy for liver diseases.

Silymarin vs. placebo for the treatment of NASH

- Single-centre, randomized, double-blinded, placebo-controlled trial

Biopsy-proven NASH patients

NAFLD activity score (NAS) ≥4
Cirrhosis excluded

- Lifestyle advice + Silymarin 700 mg t.i.d.
- Lifestyle advice + Placebo

Week -4
Week 0 Randomized 1:1
Week 48 Repeat liver biopsy

Chan WK et al, Clin Gastroenterol Hepatol 2017
Silymarin vs. placebo for the treatment of NASH

Intention-to-treat analysis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Silymarin</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary efficacy outcome</td>
<td>32.7%</td>
<td>21%</td>
<td>0.467</td>
</tr>
<tr>
<td>Steatosis</td>
<td>18.4%</td>
<td>26%</td>
<td>0.361</td>
</tr>
<tr>
<td>Lobular inflammation</td>
<td>32.7%</td>
<td>30%</td>
<td>0.776</td>
</tr>
<tr>
<td>Hepatocyte ballooning</td>
<td>40.8%</td>
<td>34%</td>
<td>0.483</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>22.4%</td>
<td>6%</td>
<td>0.023</td>
</tr>
</tbody>
</table>

Chan WK et al, Clin Gastroenterol Hepatol 2017
Sodium-glucose co-transporter 2 (SGLT-2) inhibitor

- Blocks reabsorption of glucose in the kidney, increase glucose excretion, and lower blood glucose levels
- Adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus
Empagliflozin for treatment of NASH in T2DM patients

- Investigator-initiated, single-arm, open-label pilot study

- T2DM patients with biopsy-proven NASH
  - Non-cirrhotic
  - Not already on SGLT-2, GLP-1 or TZD
  - HbA1c > 6.5%
  - Less than 65 years old

- Empagliflozin 25 mg daily

- Week 0
- Week 24
  - Repeat liver biopsy

Lai LL, Chan WK et al, Submitted for publication.
Empagliflozin vs. historical placebo

78 patients with diabetes mellitus underwent liver biopsy for suspected NASH and advanced fibrosis

12 patients did not have NASH

66 patients with biopsy-proven NASH

33 patients did not meet inclusion criteria for the study: Cirrhotic, 2 On SGLT2i, GLP1 agonist or TZD, 18 Age > 65 years old, 12 HbA1c < 6.5%, 1

33 patients were suitable for the study

24 patients excluded from the study: Considered for another clinical trial, 14 Declined to participate, 10

9 patients were included for the study

Lai LL, Chan WK et al, Submitted for publication.
## Empagliflozin vs. historical placebo

<table>
<thead>
<tr>
<th></th>
<th>Median change</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, kg/m²</td>
<td>-0.7</td>
<td>0.011</td>
</tr>
<tr>
<td>WC, cm</td>
<td>-3</td>
<td>0.033</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>-9</td>
<td>0.024</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>-6</td>
<td>0.033</td>
</tr>
<tr>
<td>FBS, mmol/L</td>
<td>-1.7</td>
<td>0.008</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>-0.5</td>
<td>0.011</td>
</tr>
<tr>
<td>GGT, U/L</td>
<td>-19</td>
<td>0.013</td>
</tr>
<tr>
<td>Volumetric liver fat fraction, %</td>
<td>-7.8</td>
<td>0.017</td>
</tr>
<tr>
<td>Steatosis grade</td>
<td>-1</td>
<td>0.014</td>
</tr>
<tr>
<td>Ballooning grade</td>
<td>-1</td>
<td>0.034</td>
</tr>
<tr>
<td>Fibrosis stage</td>
<td>0</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Lai LL, Chan WK et al, Submitted for publication.
Empagliflozin vs. historical placebo

<table>
<thead>
<tr>
<th>Category</th>
<th>Empagliflozin</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steatosis improvement</td>
<td>67% (6/9)</td>
<td>26% (13/50)</td>
<td>0.025</td>
</tr>
<tr>
<td>Lobular inflammation improvement</td>
<td>30% (2/9)</td>
<td>34% (15/50)</td>
<td>1.000</td>
</tr>
<tr>
<td>Hepatocellular ballooning improvement</td>
<td>78% (7/9)</td>
<td>22% (17/50)</td>
<td>0.024</td>
</tr>
<tr>
<td>NASH resolution without worsening fibrosis</td>
<td>44% (4/9)</td>
<td>22% (11/50)</td>
<td>0.102</td>
</tr>
<tr>
<td>Fibrosis improvement</td>
<td>44% (4/9)</td>
<td>38% (3/50)</td>
<td>0.008</td>
</tr>
<tr>
<td>Fibrosis resolution</td>
<td>38% (3/8)</td>
<td>8% (3/37)</td>
<td>0.059</td>
</tr>
<tr>
<td>Progression to cirrhosis</td>
<td>0% (0/6)</td>
<td>6% (3/50)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Lai LL, Chan WK et al, Submitted for publication.
### Subject 001

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver biopsy length, mm</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Number of portal tracts</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Steatosis grade</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Lobular inflammation grade</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Hepatocyte ballooning grade</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fibrosis stage</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>NASH</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Lai LL, Chan WK et al, Submitted for publication.
Subject 001

Pre-treatment (H&E 5x):
Grade 2 Steatosis

Pre-treatment (H&E 20x):
Focal hepatocyte ballooning and inflammation

Pre-treatment (Masson-Trichrome 10x):
Focal zone 3 perisinusoidal fibrosis (score 1a)

Lai LL, Chan WK et al, Submitted for publication.
Cascade of interventions

Treatment for metabolic syndrome

Lifestyle intervention ± pharmacological therapy
Bariatric procedure for select patients

Anti-inflammatory

Anti-fibrotic

Simple steatosis  NASH +/- advanced fibrosis  Cirrhosis
Cascade of interventions

Treatment for metabolic syndrome

Lifestyle intervention ± pharmacological therapy
Bariatric procedure for select patients

- Liraglutide
- Elafibranor

Anti-inflammatory

- Vitamin E
- Pioglitazone
- Obeticholic acid

Anti-fibrotic

- Selonsertib
- Silymarin
- Cenicriviroc

Empagliflozin
Case 1

- 44 years old Indian man
- Underlying diabetes mellitus, hypertension and dyslipidemia
- Metformin 850 mg bd, Diamicron MR 60 mg daily, Perindopril 8 mg daily, Simvastatin 20 mg at night
- Referred for ultrasonographic findings of fatty liver
- BMI 25.4 kg/m²
- BP 138/88 mmHg
- TG 1.7 mmol/L, TC 4.9 mmol/L, HDL 1.12 mmol/L, LDL 3.01 mmol/L
- FBS 9.6 mmol/L, HbA1c 9.6%
- Albumin 39 g/L, Bilirubin 17 µmol/L, ALP 105 U/L, ALT 42 U/L, AST 23 U/L, GGT 83 U/L
- Platelet 280 x 10⁹/L
- No alcohol or traditional medication
- HBs Ag negative, anti-HCV negative
Case 1

NAFLD fibrosis score
Online calculator

Angulo P, Hui JM, Marchesini G et al. The NAFLD fibrosis score
A noninvasive system that identifies liver fibrosis in patients with NAFLD

Age (years) 44
BMI (kg/m²) 25.4
IGF/diabetes
AST 23
ALT 52
Platelets (x10⁹/l) 280
Albumin (g/l) 39

Score -2.306

< -1.455: predictor of absence of significant fibrosis (F0-F2 fibrosis)
≥ -1.455 to ≤ 0.675: indeterminate score
> 0.675: predictor of presence of significant fibrosis (F3-F4 fibrosis)

BMI: body mass index
IGF: impaired fasting glucose
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
- 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 86 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 1.33 mmol/L, LDL 2.66 mmol/L
  - FBS 5.9 mmol/L, HbA1c 5.4 %
  - HBs Ag negative, anti-HCV negative
- US showed fatty liver
Case 2

### NAFLD fibrosis score

**Online calculator**

Angulo P, Hui JM, Marchesini G et al. *The NAFLD fibrosis score: A noninvasive system that identifies liver fibrosis in patients with NAFLD*  

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28</td>
</tr>
<tr>
<td>IGF/diabetes</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>62</td>
</tr>
<tr>
<td>ALT</td>
<td>111</td>
</tr>
<tr>
<td>Platelets (x10⁹/l)</td>
<td>286</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>40</td>
</tr>
</tbody>
</table>

**Score**: -2.50

- < -1.455: predictor of absence of significant fibrosis (F0-F2 fibrosis)
- ≤ -1.455 to ≤ 0.675: indeterminate score
- > 0.675: predictor of presence of significant fibrosis (F3-F4 fibrosis)

BMI: body mass index  
IGF: impaired fasting glucose
Case 2

- 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
Case 3

- 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 3

- 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 undetected, anti-HCV undetected
NAFLD fibrosis score
Online calculator

Angulo P, Hui JM, Marchesini G et al. The NAFLD fibrosis score
A noninvasive system that identifies liver fibrosis in patients with NAFLD

Age (years) 48
BMI (kg/m²) 29.9
IGF/diabetes
AST 87
ALT 118
Platelets (×10⁹/l) 168
Albumin (g/l) 36
Score 0.212

< -1.455: predictor of absence of significant fibrosis (F0-F2 fibrosis)
≤ -1.455 to ≤ 0.675: indeterminate score
> 0.675: predictor of presence of significant fibrosis (F3-F4 fibrosis)

BMI: body mass index
IGF: impaired fasting glucose
<table>
<thead>
<tr>
<th>CAP (dB/m)</th>
<th>E (kPa)</th>
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<tbody>
<tr>
<td>IQR</td>
<td>18</td>
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<tr>
<td>MEDIAN</td>
<td>358</td>
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Exam M (Liver)
Operator: CHAN WAH KHEONG
Valid measurements: 10
Total measurements: 10

Indication: NAFLD
Case 3

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

- The landscape of therapeutic options for NAFLD is rapidly evolving
- It is important that NAFLD patients be carefully assessed for the severity of their liver disease so that appropriate management decisions can be made
- More studies are needed
- Non-pharmacological management and public health approach are equally important
Thank you