Community Assessment of liver fibrosis in Primary Care & Rural Settings

Dr Anne Balcomb  GP Orange. NSW
Disclaimers

- 2016 Bristol Myers Squibb - supported attendance educational HCV meeting Sydney

- 2015 Gilead - supported attendance 2015 to think tank on Hep C models care in Melbourne
Primary Care Challenges

- Upskilling all Australian GP’s re:
  1. Fibrosis assessment options
  2. Importance of diagnosing advanced liver disease
  3. DAA’s and supporting more GP’s to prescribe

- Limited Fibroscan access
Extra Rural Challenges

- Limited Fibroscan & imaging access
- Travel distances & poor public transport
- Specialist & investigation costs - few public gastroenterology clinics
- Lack of gastroenterologists & long waiting lists >6 mths
- Stigma living with HCV
- Shortage/high turnover of GP’s in some settings
Rural Advantages

- Specialists known & readily available for advice
- Clients well known & trust GP’s
- Outreach Fibroscan clinics
- Used to dealing with complex chronic conditions
- Keen to upskill and take on challenges
Challenges to diagnosing advanced liver disease/cirrhosis

No single test can reliably diagnose all cases of cirrhosis
Piece the clues together

- Patient history
- Physical examination
- Pathology
- Imaging - abdominal ultrasound
- Fibroscan
- APRI score
- FIB 4 Index
Clue 1 to Advanced Fibrosis

**Medical history**

- **Duration hepatitis C infection**  
  RED FLAGs >15/20 yrs duration infection

- **Age patient & gender**  
  RED FLAGs > 40 yrs & male

- **Co-infections** (HIV, Hep B)

- **Co-morbidities** (diabetes, obesity)

- **Drug & ETOH history** (daily heavy/regular binging)
Clue 2 - Advanced Fibrosis

**Physical examination**

- Stigmata CLD - spider naevi, palmar erythema
- Enlarged liver/spleen
- Signs of decompensation - ascites, peripheral oedema, muscle wasting, hepatic encephalopathy
Clue 3 - Advanced Fibrosis

**Pathology results**

- AST higher than ALT (AST/ALT ratio >1)

- Platelet count low <150 (trending down over few yrs)

- Clues to heavy ETOH (elevated GGT & AST)

- Low albumin

- APRI score

- FIB 4 Index
Clue 4 - Advanced Fibrosis

**Imaging**

- Abdominal ultrasound (splenomegaly, irregular liver outline, enlarged portal vein/portal hypertension, ascites)

- Fibroscan
Clue 5  Fibroscan - current gold standard

**Advantages**
- Non invasive & quick
- Portable
- Good indicator of no fibrosis or cirrhosis
- XL probe for those overweight

**Disadvantages**
- Cannot obtain result in all
- Limitations staging F2/F3
- Operator dependent
- Need to fast
- Expensive + annual calibration fee probe ($10,000/probe)
- Nil item number
- Limited access for primary care practitioners
- Falsely elevated readings - acute inflammation etc.
Clue 6 - Blood test algorithms
e.g. APRI & FIB 4 Index

**ADVANTAGES**

- Simple
- Inexpensive
- Easily reproducible
- Immediately available during consultation
- Determine who needs referral for Fibroscan pre-treatment and who does not
- Way of monitoring liver fibrosis progression /regression over time
AST to Platelet Ratio Index (APRI)

\[
APRI = \frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}} \times 100 \times \frac{1}{\text{Platelet Count (10}^9/\text{L)}}
\]
What does an APRI score of 0.4 tell me?

- APRI has two cut-offs: a lower one (0.5) and a higher one (1.5)
- If APRI score is less than or equal to 0.5 - no fibrosis or just a little
- If APRI score is 1.5 or above - probable cirrhosis
- APRI score between 0.5 & 1.5 - related to progressive fibrosis stages (F2/3)
Australian recommendations for the management of hepatitis C infection: Consensus Statement 2016

- If APRI is <1  - Cirrhosis unlikely
- If equal or > 1  - Refer for Fibroscan
APRI Score Practical Tips

- Use AST not ALT
- Differing AST upper limit normal range via pathology labs (35 or 40)
- Use apps on phone or desktop calculators HepCalc
- Limitations
- If any cirrhosis clues refer fibroscan e.g. downtrending platelets
Fib 4 Index Formula

\[(\text{Age (years)} \times \text{AST U/L}) \times (\text{Platelet count} \times (\text{square root of ALT U/L}))\]

Advantages
- Non invasive, simple
- Factors in age
- Way to monitor fibrosis over time
- Use phone or desktop apps - HepCalc
What does a FIB 4 Index of 1 mean?

Hepatitis C Virus

FIB-4 Index < 1.45 = F0 - F1 (no fibrosis or just a little)

FIB-4 Index > 3.25 = F3 - F4 (cirrhosis likely)

FIB-4 Index 1.45-3.25 = F2 - F3

Castera et al. reported that the combination of FibroScan and FibroTest performed better than FibroScan, FibroTest, or the APRI tests alone performed in the same population.
My experience since 1st March

- 1 day per week run GP rural liver clinic
- Initially Fibroscan on loan 4 mths
- Referrals from other GP’s across region, self referral, Drug and ETOH, gastroenterologists & hospital
- Work closely gastroenterologists co-managing & starting some with cirrhosis
- 89 on treatment so far
Fibrosis assessment data collected on first 62 people started on DAA Treatment post 1\textsuperscript{st} March 2016
Fibrosis assessment - Fibroscan < 7.5 kPA

<table>
<thead>
<tr>
<th>F0-1 based on Fibroscan</th>
<th>Number Assessed</th>
<th>Number on Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroscan &lt; 7.5 KPa</td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>APRI &lt; 1</td>
<td>29 (2 &gt;1)</td>
<td>27 (2 &gt;1)</td>
</tr>
<tr>
<td>FIB 4 Index &lt;1.45</td>
<td>29 (2 &gt; 1.45)</td>
<td>27 (2 &gt;1.45)</td>
</tr>
</tbody>
</table>

No cases F0-1 would have missed

Those with APRI >1 or FIB 4 >1.45 had a Fibroscan (low platelets due to ITP)
## Fibrosis assessment - Fibroscan 7.5-12.4 kPa

<table>
<thead>
<tr>
<th>F2-3 based on Fibroscan</th>
<th>Number Assessed</th>
<th>Number on Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroscan 7.5 -12.4 KPa</td>
<td>17</td>
<td>15</td>
</tr>
</tbody>
</table>
| APRI                        | 13 <1
4 >1           | 11 <1
4 >1           |
| FIB 4 Index >1.45           | All >1.45
16 < 3.25
1 >3.25         | All >1.45
14 < 3.25
1 >3.25         |

Was Fibroscan assessment incorrect & 1-2 cases of cirrhosis missed? Maybe ......and both GT 3a
Cirrhosis based on Fibroscan > 12.5 kPa

<table>
<thead>
<tr>
<th>F4 based on Fibroscan</th>
<th>Number Assessed</th>
<th>Number on Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroscan &gt; 12.5 KPa</td>
<td>20</td>
<td>18</td>
</tr>
<tr>
<td>APRI Score</td>
<td>18 &gt;1&lt;br&gt;2 &lt;1</td>
<td>17 &gt;1&lt;br&gt;1 &lt;1</td>
</tr>
<tr>
<td>Fib 4 Index</td>
<td>All &gt; 2 (All &gt;1.45) &lt;br&gt;1 &gt; 3.25 &lt;br&gt;7 &lt; 3.25</td>
<td>All &gt; 2 (All &gt;1.45) &lt;br&gt;11 &gt; 3.25 &lt;br&gt;7 &lt; 3.25</td>
</tr>
</tbody>
</table>

2 cases APRI <1 if used alone....would have missed cirrhosis

If combine APRI >1 with FIB 4 Index >1.45 to refer for Fibroscan then no cases cirrhosis would have been missed
If combine APRI >1 + FIB 4 >2 as cut off Fibroscan referral

- No cirrhosis cases would have been missed

- Could have prevented 31 out 62 Fibroscans on those commenced on treatment (50% cases)

- Have commenced 9 on treatment where APRI < 1 and FIB 4 < 1.45 without Fibroscan
Use all the clues

Maybe combine APRI and/or FIB 4 Index with Fibroscan for all
Case 1  Commenced gastroenterologist 12 weeks SOF/DAC

- 48 yr male
- GT 3a
- Treatment experienced
- AST 165, ALT 184
- Plat 173
- Fibroscan 10.8 kPA (told initial reading >12 but repeated)
- APRI 3.039  (>1.5 cirrhosis likely)
- FIB 4  3.37  (>3.25 cirrhosis likely)
Case 2 - Treated 12 weeks SOF/DAC

- 53 female
- GT 3a
- Treatment Naïve
- ALT 98
- AST 88
- Plat 152
- Fibroscan 6.1 KPa
- APRI Score 1.65 (>1.5 cirrhosis likely)
- FIB 4 Index 3.1 (>3.25 cirrhosis likely)
Case 3 - Treated 12 weeks LED/SOF

- 53 yr female
- GT 1a
- Treatment Naïve
- ALT 29, AST 54
- Plat 214
- APRI 0.721 (< 1 cirrhosis unlikely)
- FIB 4 Index 2.48 (1.45-3.25 = F2-F3)
- Fibroscan 38.5 kPa

Note ETOH 3-5 standard/day
PANEL DISCUSSION
What to do?

- Fibroscan 12.3 kPa, APRI =1.7 & FIB 4 = 2.6
  Female aged 38 GT 3a  (what if GT1)

- Fibroscan 11.9 kPA, APRI 2.2 & FIB 4 is 3.5
  Male aged 50 GT 3a  (what if GT1)

When to classify and treat as cirrhosis?