

Community Assessment of liver fibrosis in Primary Care & Rural Settings



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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 Fibrosan & 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)


$$\text{APRI} = \frac{\frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}}}{\text{Platelet Count (10}^9\text{/L)}} \times 100$$

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

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

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)

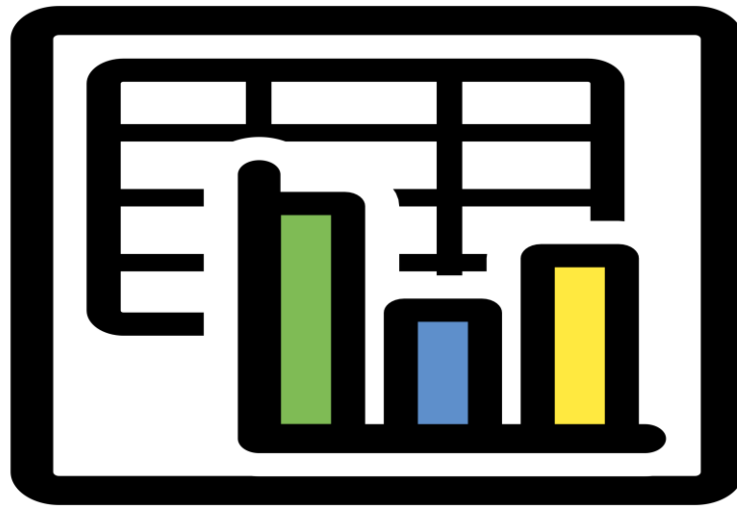
FIB-4 Index 1.45-3.25 = F2 - F3

- ▶ 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 1st March 2016



Fibrosis assessment - Fibroscan < 7.5 kPa

F0-1 based on Fibroscan	Number Assessed	Number on Treatment
Fibroscan < 7.5 KPa	31	29
APRI < 1	29 (2 >1)	27 (2 >1)
FIB 4 Index <1.45	29 (2 > 1.45)	27 (2 >1.45)

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

F2-3 based on Fibroscan	Number Assessed	Number on Treatment
Fibroscan 7.5 -12.4 KPa	17	15
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 ?
Maybeand both GT 3a

Cirrhosis based on Fibroscan > 12.5 kPa

F4 based on Fibroscan	Number Assessed	Number on Treatment
Fibroscan > 12.5 KPa	20	18
APRI Score	18 >1 2 <1	17 >1 1 <1
Fib 4 Index	All > 2 (All >1.45) 1 > 3.25 7 < 3.25	All > 2 (All >1.45) 11 >3.25 7 <3.25

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?