Liver fibrosis assessment in resource-limited countries

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AIDS 2014
STEPPING UP THE PACE
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Why should we assess liver fibrosis in resource-limited settings ?

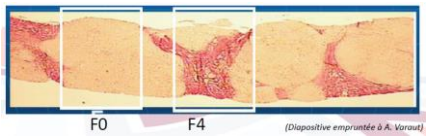
- Liver fibrosis = « surrogate » marker of liver function;
- Most international recommandations on viral hepatitis care and management are based on liver fibrosis F2 stage to initiate treatment, whatever the virus;
- Crucial for screening cirrhosis and complications of cirrhosis

Tools for fibrosis evaluation

- Liver biopsy: still considered as a gold standard
- Simple biochemical scores: Fib4, APRI
- Complex biochemical scores: fibrotest, fibrometre, hepascore
- Elastometry (Fibroscan®)

Use of liver biopsy in RLS

- **Crucial for diagnosis of tumoral / infectious / metabolic diseases**
- Subject to economic restrictions (500-1000€ in France)
- Subject to human resources restrictions (hepatologists, pathologists…)
- Intrinsic limitations: tolerance issues, repeatability issues, sample variability



Non invasive tests: advantages and drawbacks

Test	Components	Requirements	Cost
APRI	AST, platelets	Simple serum and haematology tests	+
FIB4	Age, AST, ALT, platelets	Simple serum and haematology tests	+
Fibrotest	gGT, haptoglobin, bilirubin, A1 apolipoprotein, α2-macroglobulin	Specialized tests. Testing at designated laboratories	++
Fibroscan	Transient elastography	Dedicated equipment	+++

- Adavantages: easy to use, can be repeated, some of them very cheap
- Drawbacks: not 100% performance, susceptible to underlying disease, should not be used in treated patients, may not be accurate in cured patients with residual fibrosis/cirrhosis

Performance of APRI and Fib4 (1)

$$\text{APRI} = \frac{[(\text{AST (IU/L)} / \text{AST\_ULN (IU/L)}) \times 100]}{\text{platelet count } (10^9/\text{L})}$$

$$\text{FIB4} = \frac{\text{age (yr)} \times \text{AST(IU/L)}}{\text{platelet count } (10^9/\text{L}) \times [\text{ALT(IU/L)}^{1/2}]}$$

- Studies performed in Africa: Senegal, Burkni Faso, Gambia, Nigeria, Egypt, Tunisia, Mauritania

	APRI (low cut-off)	APRI (high cut-off)	FIB4 (low cut-off)	FIB4 (high cut-off)
Significant fibrosis (METAVIR ≥F2)	0.5	1.5	1.45	3.25
Cirrhosis (METAVIR F4)	1.0	2.0	–	–

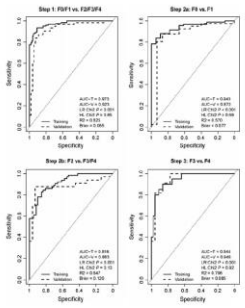
Performance of APRI and Fib4 (2)

		APRI (low cut-off)	APRI (high cut-off)	FIB4 (low cut-off)	FIB4 (high cut-off)
Significant fibrosis (METAVIR ≥F2)	Sensitivity (95% CI)	82 (77–86)	39 (32–47)	89 (79–95)	59 (43–73)
	Specificity (95% CI)	57 (49–65)	92 (89–94)	42 (25–61)	74 (56–87)
Cirrhosis (METAVIR F4)	Sensitivity (95% CI)	77 (73–81)	48 (41–56)	–	–
	Specificity (95% CI)	78 (74–81)	94 (91–95)	–	–

Adapted from WHO Guidelines on HCV in RLS (2014), meta-analysis

Other biochemical scores

- Combination of Hyaluronic Acid, TGF-β1, α2-macroglobulin, MMP-2, Apolipoprotein-A1, Urea, MMP-1, alpha-fetoprotein, haptoglobin, RBCs, haemoglobin and TIMP-1
- High performance in fibrosis staging
- Formula freely provided by Egyptian colleagues



El Kamary, Liver Int 2013

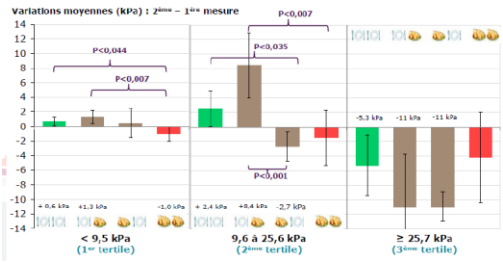
Performance of Fibroscan®

	Transient elastography (Fibroscan)
Significant fibrosis (METAVIR ≥F2)	7–8.5 kPa
Cirrhosis (METAVIR F4)	11–14 kPa

		Transient elastography (Fibroscan)
Significant fibrosis (METAVIR ≥F2)	Sensitivity (95% CI)	79 (74–84)
	Specificity (95% CI)	83 (77–88)
Cirrhosis (METAVIR F4)	Sensitivity (95% CI)	89 (84-92)
	Specificity (95% CI)	91 (89–93)

Adapted from WHO Guidelines on HCV in RLS (2014), meta-analysis

Influence of meals of FS results



Cales P. AFEF meeting 2012

Comparison of NILT for cirrhosis in the context of Africa

- Prolifica study: Prevention of cancer and liver cirrhosis in Africa (Gambia, PI: Pr M. Thursz)
- 116 HBV-newly diagnosed patients with LB and a battery of NILT including FS

	F0-3 vs F4
FIBROSCAN	
AUROC (95% CI)	**0.97 (0.94-1)**
APRI	
AUROC (95% CI)	0.79 (0.66-0.92)
FIB-4	
AUROC (95% CI)	0.80 (0.69-0.92)
Comparison of AUROC	
FS *vs* APRI	p=0.007
FS *vs* FIB-4	p=0.004
APRI *vs* FIB-4	p=0.8

Lemoine M. EASL 2014

HCV Guidelines based on NILTs in resource-limited countries

- Treatment decision is not based of the liver fibrosis severity
- But because of potential financial constraints for access to treatment, evaluating liver fibrosis is important to help heathcar providers in their decision of who to treat
- Also important to screen for cirrhosis because of specific clinical management

WHO, Guidelines for the screening, care nd treatment of persons with HCV. 2014

HBV Guidelines based on NILTs in resource-limited countries

- Not all HBsAg+ persons should be treated (inactive carriers, immunotolerant, etc.
- Priority for treatment: cirrhotic patients
- Best ratio between affordability/performance = APRI for cirrhosis screening
- APRI with other virological markers used to determine which patient should be offered treatment
- FS is recommanded whenever it is accessible

WHO, Guidelines for HBV care and management – Work in Progress