



# Biological Non-Invasive Tests for Prediction of Liver Fibrosis in HIV-HCV coinfecting patients: ANRS Co3 Aquitaine Cohort



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## BACKGROUND

• Several biological non-invasive tests providing a scoring system after combination of routine laboratory parameters have been proposed as alternative to liver biopsy to predict liver fibrosis in HCV monoinfected patients (1,2,3,4,5).

• In HIV-HCV coinfecting patients specifically, very few models have been proposed but have not been yet validated. Models already validated in HCV monoinfected patients may have low accuracy in HIV-HCV coinfecting patients (6,7,8).

## AIM

• To validate, in HIV-HCV coinfecting patients of the ANRS Co3 Aquitaine Cohort, 4 predictive models of liver fibrosis developed in HCV monoinfected (APRI, Forns Index and platelet count-based) and in HIV-HCV coinfecting patients (FIB-4).

## PATIENTS

• 200 HIV/HCV coinfecting patients were studied.

• All patients underwent liver biopsy between 1999 and 2005 and had complete biological data to validate all the considered tests.

• Exclusion criteria were :

- positive hepatitis B surface antigen
- alcohol consumption exceeding 20g/d

## REFERENCES:

(1) Lackner C et al. *Hepatology* 2005 ; (2) Snyder N et al. *J Clin Gastroenterol* 2006 ; (3) Forns X et al. *J Hepatology* 2002 ; (4) Wai CT et al. *Hepatology* 2003 ; (5) Castera L et al. *Gastroenterology* 2005 ; (6) Sterling RK et al. *Hepatology* 2006 ; (7) Kelleher TB et al. *Hepatology* 2005 ; (8) Macias J et al. *Gut* 2006 ; (9) Bedossa P et al. *Hepatology* 1996

## METHODS

• Biological data were available on the date of liver biopsy for 55% of patients and within 1 month of the date of liver biopsy for 45%.

• Liver fibrosis was assessed on liver biopsy using METAVIR scoring system (gold standard) (9).

• Forns, APRI and FIB4 scores were calculated using the models originally described :

Forns (3) :  $7,811 \cdot 3,131 \cdot \ln(\text{platelets}) + 0,781 \cdot \ln(\text{GGT}) + 3,467 \cdot \ln(\text{age}) - 0,014 \cdot (\text{cholesterol})$  ; APRI (4):  $(\text{AST}(\text{IU/L}) / \text{ULN}) \times 100 / \text{platelets}$  ; FIB4 (6) :  $(\text{age} \times \text{AST}) / (\text{platelets} \times \text{ALT}^{1/2})$ .

• Diagnostic performance was estimated for each test by measuring the area under the ROC curve (AUROC), sensitivity (Se), specificity (Sp), positive (PPV) and negative (NPV) predictive values. The percentage of patients correctly identified (PCI) was also calculated.

## RESULTS

### Characteristics of the 200 HIV/HCV coinfecting patients

Age (yrs) (mean±SD)	39.8 (6.3)
Gender (male) n(%)	133 (66.5)
BMI (kg/m <sup>2</sup> ) (mean±SD)	22.1 (3.2)
Source of HCV infection n(%)	
IV drug use	136 (68)
Platelets count (10 <sup>9</sup> /l) (mean±SD)	188 (67)
T CD4 count (cells/μl) n (%)	
≤ 200	11 (6.1)
> 200	168 (93.9)
HIV plasma RNA undetectable n (%)	84 (49)
Liver fibrosis n (%)	
F0-F1	43 (21.5)
F2	87 (43.5)
F3	31 (15.5)
F4	39 (19.5)

### AUROC and diagnostic performance of the models aimed at predicting significant fibrosis (F2-F4)

	Fibrosis stage											
	APRI	N=200 n (%)	F0-F1 N=(43) n (%)	F2-F4 N=(157) n (%)	Se (%)	Spe (%)	PPV (%)	NPV (%)	AUROC C (%)	PCI (%)		
≤ 0.5	63	(31.5)	28	(65)	35	(22)	77.7	65.1	89	44.4	77	35.5
>0.5	137	(68.5)	15	(35)	122	(78)						
<1.5	156	(78)	42	(98)	114	(73)						
≥ 1.5	44	(22)	1	(2)	43	(27)	27.4	97.7	97.7	26.9		

	Fibrosis stage											
	Forns	N=153 n (%)	F0-F1 N=(26) n (%)	F2-F4 N=(127) n (%)	Se (%)	Spe (%)	PPV (%)	NPV (%)	AUROC C (%)	PCI (%)		
≤ 4.2	30	(20)	9	(35)	21	(17)	83.5	34.6	86.2	30	75	19
>4.2	123	(80)	17	(65)	106	(83)						
<6.9	124	(81)	26	(100)	98	(77)						
≥ 6.9	29	(19)	0	(0)	29	(23)	22.8	100	100	100	21	

Se: sensitivity; Spe: specificity; PPV: positive predictive value; NPV: negative predictive value; PCI: patients correctly identified; AUROC: area under the receiver operating characteristic curve

### AUROC and diagnostic performance of the model aimed at predicting severe fibrosis (F3-F4)

	Fibrosis stage											
	FIB4	N=200 n (%)	F0-F2 N=(130) n (%)	F3-F4 N=(70) n (%)	Se (%)	Spe (%)	PPV (%)	NPV (%)	AUROC C (%)	PCI (%)		
≤ 1.45	110	(55)	91	(70)	19	(27)	72.9	70	56.7	82.7	77	56.5
> 1.45	90	(45)	39	(30)	51	(73)						
< 3.25	169	(84.5)	121	(93)	48	(69)						
≥ 3.25	31	(15.5)	9	(7)	22	(31)	31.4	93.1	71	71.6		

Se: sensitivity; Spe: specificity; PPV: positive predictive value; NPV: negative predictive value; PCI: patients correctly identified; AUROC: area under the receiver operating characteristic curve

### AUROC and diagnostic performance of the models aimed at predicting cirrhosis (F4)

	Fibrosis stage											
	APRI	N=200 n (%)	F0-F3 N=(161) n (%)	F4 N=(39) n (%)	Se (%)	Spe (%)	PPV (%)	NPV (%)	AUROC C (%)	PCI (%)		
≤ 1	124	(62)	115	(71)	9	(23)	76.9	71.4	39.5	92.7	80	65.5
> 1	76	(38)	46	(29)	30	(77)						
< 2	170	(85)	147	(91)	23	(59)						
≥ 2	30	(15)	14	(9)	16	(41)	41	91.3	53.3	86.5		

	Fibrosis stage									
	Platelet count	N=200 n (%)	F0-F3 N=(161) n (%)	F4 N=(39) n (%)	Se (%)	Spe (%)	PPV (%)	NPV (%)	AUROC C (%)	PCI (%)
≤ 130	37	(18.5)	14	(9)	59	91.3	62	90	78	85
≥ 130	163	(81.5)	147	(91)						

Se: sensitivity; Spe: specificity; PPV: positive predictive value; NPV: negative predictive value; PCI: patients correctly identified; AUROC: area under the receiver operating characteristic curve

## CONCLUSION

• Diagnostic performance of APRI was good for cirrhosis in HIV-HCV coinfecting patients, but not as good as platelet count (65.5% and 85% of patients correctly classified, respectively) questioning its relevance in clinical practice.

• Conversely, diagnostic performance of APRI and Forns was poor for significant fibrosis (35.5% and 19% of patients correctly classified, respectively) and then should not be applied routinely in HIV-HCV coinfecting patients.

• Finally, our results confirm the good diagnostic performance of FIB4 for severe fibrosis (56.5% of patients correctly classified) in HIV-HCV coinfecting patients.