Independent comparison of 4 blood scores of liver fibrosis in chronic hepatitis C: FibroMeter, Fibrotest, Hepascore, and APRI

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Introduction

Blood tests can be classified into 4 categories: simple tests made of a few indirect markers without algorithm like APRI, indirect scores including indirect markers composite of an algorithm like Fibrotest (FT), direct scores including direct markers composite of an algorithm like ELF score, and mixed scores including indirect and direct markers composite of an algorithm like FibroMeter (FM) and Hepascore (HS).

The main aim of this study was to perform an external independent evaluation of these mixed scores by comparison with APRI as simple test and FT as indirect score. Direct scores were not evaluated since they include direct markers either with a low performance or that are not available in routine.

Patients

356 patients with C chronic hepatitis attending the hepato-gastroenterology unit of the University Hospital in Tours, and several centers (2 University Hospital, 1 public hospital, 2 private clinics) from Provence - Côte d'Azur (PACA) area, France.

Methods

Blood dosages

Analyses of blood samples provided the following variables: platelet (PLT) count, urea, bilirubin, gammaglutamyl transpeptidase (GGT), aspartate (AST), and alanine (ALT) aminotransferases, prothrombin index (PI), apolipoprotein A1 (ApoA1), haptoglobin, hyaluronic acid (HA), and alpha-2-macroglobulin (A2M).

Liver biopsy

Fibrosis was staged by two independent pathologists according to the Metavir staging.

Results

General characteristics

These characteristics are presented in table 1. The 2 populations were significantly different: Tours population was younger and with a less severe hepatitis with a prevalence of clinically significant fibrosis (CSF) of 31% vs 49% in PACA (p=0.001).

Test performance

The statistical comparison of performance between tests is available with AUROC and is presented in table 2.

CSF includes F2 + F3 + F4, severe fibrosis includes F3 + F4, and cirrhosis includes F4.

Pattern of test according to F stage

Figure 1 is the box plots of blood tests for CSF probability as a function of Metavir fibrosis stage.

Test performance profile (TPP) was assessed between the two tests with the nearest and highest AUROCs, i.e. FM and FT.

Results

Figure 2 clearly shows a significantly different TPP between FM and FT. FT was superior to FM for F1 stage whereas FM was superior to FT for F2, F3, and F4 stages.

Table 1. General characteristics of patient populations.

	Whole population	Provence-Côte d'Azur	Tours	p
N patients	356	198	158	-
Sex (% male)	189 (53)	99 (50)	90 (57)	0,23
Age (year)	44,9 ± 12,9	48,1 ± 13,7	40,9 ± 10,5	0,01
Metavir fibrosis stage:				
F0 (%)	15 (4)	9 (4)	6 (4)	0,79
F1 (%)	195 (55)	92 (48)	103 (65)	0,002
F2 (%)	95 (26)	61 (31)	34 (22)	0,08
F3 (%)	38 (11)	25 (12)	13 (8)	0,29
F4 (%)	13 (4)	11 (6)	2 (1)	0,07
Clinically significant fibrosis (%)	146 (41)	97 (49)	49 (31)	0,001
Severe fibrosis (%)	51 (14)	36 (18)	15 (9,5)	0,02
Metavir fibrosis score	1,5 ± 0,9	1,7 ± 0,9	1,4 ± 0,7	0,001
Liver specimen length (mm)	22,0 ± 7,1	23,3 ± 7,3	20,5 ± 6,4	0,04
Median liver biopsy date	january 15 2003	may 20 2003	april 8 1999	<,0001
Platelets (G/L)	211,2 ± 65,0	203,2 ± 60,3	221,2 ± 69,2	0,64
Prothrombin index (%)	92,8 ± 7,6	92,1 ± 7,7	93,7 ± 7,4	0,03
ASAT (UI/L)	49,3 ± 37,3	57,3 ± 42,7	39,2 ± 26,0	<,0001
ALAT (UI/L)	76,5 ± 66,2	77,7 ± 71,3	74,9 ± 59,3	0,99
GGT (UI/L)	67,1 ± 108,7	75,0 ± 117,3	57,3 ± 96,5	0,10
Bilirubin (µmol/L)	10,5 ± 5,3	9,9 ± 5,5	11,0 ± 5,0	0,03
Urea (mmol/L)	5,8 ± 1,6	6,0 ± 1,8	5,6 ± 1,3	0,11
Apolipoprotein A1 (g/L)	1,5 ± 0,4	1,5 ± 0,4	1,4 ± 0,4	0,05
Haptoglobin (g/L)	0,94 ± 0,45	0,93 ± 0,45	0,96 ± 0,46	0,59
Alpha2 macroglobulin (mg/dL)	287 ± 111	272 ± 91	305 ± 130	0,10
Hyaluronate (µg/L)	52,4 ± 96,2	64,9 ± 114,7	36,7 ± 63,2	<,0001

Table 2. AUROC as a function of blood score and fibrosis cut-off.

	FT	FM	APRI	HS	p
≥ F2	0.79	0.78	0.76	0.76	NS
≥ F3	0.81	0.85	0.81	0.81	NS
F4	0.86	0.94	0.92	0.89	NS

Results

Figure 1. Box plots of blood tests as a function of Metavir fibrosis stage for probability of clinically significant fibrosis (CSF)

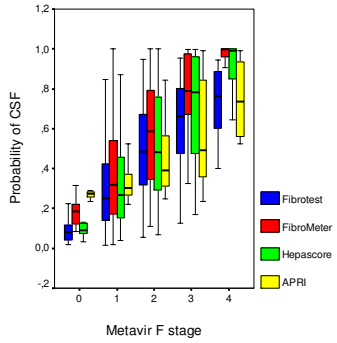
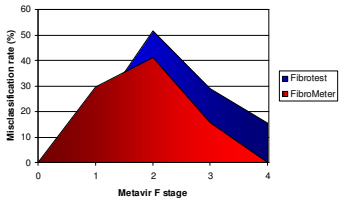


Figure 2. Test performance profile: comparison of misclassification rate for clinicalle significant fibrosis between FM and FT



Conclusions

In conclusion, this study shows a good performance of blood tests but lesser than in the original publications. We have used a new method to compare the diagnostic accuracy as a function of fibrosis stage. This pattern is called test performance profile and shows significant differences in diagnostic accuracy between blood tests as a function of fibrosis stage. This test performance profile should be added in the description of test performance especially in comparative study.