Combination of Non Invasive Markers (Fibrotest, Hepascore, APRI, and Forns) to Identify Liver Fibrosis in HCV-Infected Patients and to Avoid Liver Biopsy

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Introduction

Liver biopsy is recommended for the management of hepatitis C virus (HCV) infected patients. Many studies have been performed to evaluate the use of readily available laboratory tests to predict significant fibrosis or cirrhosis and substantially reduce the number of biopsies performed.

The aim of this study was to validate a new available score for fibrosis and cirrhosis prediction 'Hepascore' (Hep) by comparing its diagnostic values with Fibrotest (FT), and to create a decisionnal algorithm by combining Hepascore, FT, APRI, and Forns score.

Patients & Methods

467 HCV infected patients were retrospectively included from a French multicenter independent study. Hep, FT, APRI, and Forns scores were assessed and compared with liver histology done on the same day.

ROC curve analysis was used to measure scores accuracies. Hanley-Mcneil test was used to compare AUCs.

Results

Table 1 shows clinical and biological characteristics of the 467 patients.

Table1: Clinical and biochemical characteristics of the 467 patients

Mean (SD) age, years	47 (12)
Male, n(%)	274 (59%)
Liver Biopsy Stage, n(%)	
F0	68 (15%)
F1	168 (36%)
F2	101 (22%)
F3	95 (20%)
F4	35 (7%)
Mean (SD) size, mm	19.69 (8.38)
Median Portal Tracts [Range], n	9 [2 ;36]
Mean (SD) A2M, g/L	2.67 (1.03)
Mean (SD) Haptoglobin, g/L	0.97 (0.47)
Mean (SD) APOA1, g/L	1.51 (0.35)
Mean (SD) Bilirubin, µmol/L	10.95 (5.66)
Mean (SD) GGT, IU/L	78.50 (114.33)
Mean (SD) AST, IU/L	65.91 (58.38)
Mean (SD) ALT, IU/L	74.82 (64.77)
Mean (SD) Cholesterol, mg/dL	163.81 (55.23)
Mean (SD) Platelets, G/L	209.10 (59.27)
Mean (SD) Albumins, g/L	40.78 (5.38)

231/467 (50%) patients had significant fibrosis (Metavir≥F2), 35/467 (8%) had cirrhosis (Metavir F4). Mean size of liver biopsy was 19.69 ± 8.38 mm and median number of portal tracts was 9 [range : 2 ;36].

Box plots of Hep and FT according to Metavir fibrosis stages are shown in Figure 1.

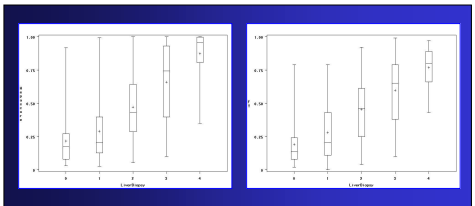

Figure 1: Box plots of Hepascore and FT according to Metavir fibrosis stages

Results

Hep AUCs for F2-F4, severe fibrosis (F3F4), and F4 diagnosis were 0.82 [95% CI : 0.79 ;0.86], 0.84 [0.80 ;0.87], and 0.90 [0.87 ;0.93] respectively, in the same range as FT : 0.83 [0.79 ;0.86], 0.84 [0.80 ;0.87], and 0.89 [0.86 ;0.93] respectively (all p-values were not significant (NS))(Figure 2).

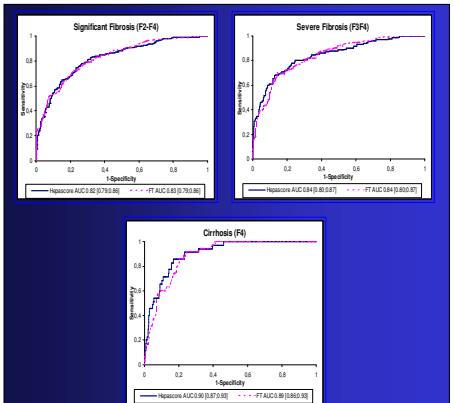

Figure 2: Hepascore and FT ROC curves for significant fibrosis (F2-F4), severe fibrosis (F3F4), and cirrhosis (F4)

All comparisons between Hepascore and FT remain not significantly different

Diagnostic values of Hep and FT for F0F1 vs F2-F4 and F0-F3 vs F4 were not different (P NS) (Table 2).

Table 2: Diagnostic values of Hepascore and FT for F2-F4, and F4 diagnosis (all p values were not significant)

	Hepascore	FT
F0F1 vs F2-F4	Cut-off :0.50	
Sensitivity, % (95% CI)	63 (57-69)	62 (58-68)
Specificity, % (95% CI)	86 (81-90)	84 (80-88)
NPV, % (95% CI)	70 (65-75)	70 (64-75)
PPV, % (95% CI)	82 (76-87)	80 (74-85)
F0-F3 vs F4	Cut-off :0.85	
Sensitivity, % (95% CI)	71 (57-83)	63 (48-76)
Specificity, % (95% CI)	88 (85-91)	88 (85-91)
NPV, % (95% CI)	97 (96-99)	97 (95-98)
PPV, % (95% CI)	33 (24-43)	29 (21-40)

Stage by stage AUCs comparison showed no significant difference between Hep and FT (Table 3).

Table 3: Hepascore and Fibrotest stage by stage AUCs comparison

Fibrosis Stages	Hepascore	Fibrotest	P
F0 vs F1	0.61 [0.54 ;0.67]	0.65 [0.59 ;0.71]	NS
F1 vs F2	0.73 [0.67 ;0.78]	0.71 [0.66 ;0.77]	NS
F2 vs F3	0.69 [0.62 ;0.76]	0.67 [0.60 ;0.74]	NS
F3 vs F4	0.74 [0.66 ;0.82]	0.71 [0.63 ;0.79]	NS
F0 vs F2	0.82 [0.75 ;0.88]	0.83 [0.77 ;0.88]	NS
F1 vs F3	0.83 [0.78 ;0.87]	0.84 [0.79 ;0.88]	NS
F2 vs F4	0.91 [0.85 ;0.95]	0.87 [0.79 ;0.92]	NS
F0 vs F3	0.89 [0.83 ;0.94]	0.91 [0.86 ;0.95]	NS
F1 vs F4	0.96 [0.92 ;0.98]	0.96 [0.93 ;0.99]	NS
F0 vs F4	0.99 [0.94 ;1]	0.98 [0.94 ;1]	NS

A new decisionnal algorithm can be proposed (Figure 3). If Hep had been done alone with FT, 387/467 (82%) patients would have been concordant. Among these 387 patients, 306 (79%) were concordant with liver biopsy.

Results

Among the 81 (21%) remaining patients, 40 (50%) had biopsy failure defined by poor quality biopsy and discordance with all tests (Hep, FT, APRI, and Forns). Therefore 346/387 (89%) patients, do not need liver biopsy.

When adding APRI and Forns to the 80/467 (18%) patients that are discordant between Hep and FT, 73 (16%) patients would be concordant between Hep and, APRI and/or Forns or between FT and, APRI and/or Forns. In these 73 patients, liver biopsy is not needed. Therefore, in 7/467 (2%) cases liver biopsy would remain necessary.

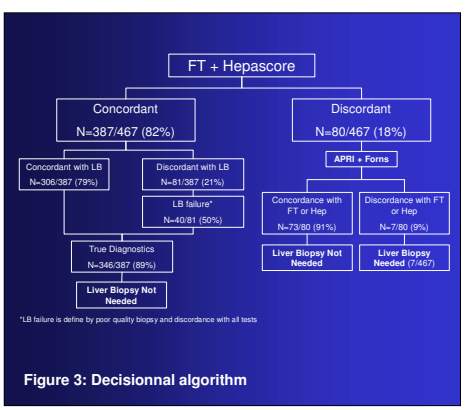

Figure 3: Decisionnal algorithm

Conclusions

Hepascore is an accurate model for fibrosis prediction. Its diagnostic performances are in the same range as Fibrotest. When combining Hepascore with Fibrotest, APRI, and Forns, liver biopsy could have been avoided in 460/467 (99%) patients.

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