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AST-platelet ratio index, Forns index and FIB-4 in the prediction of significant fibrosis and cirrhosis in patients with chronic hepatitis C

Fatih GÜZELBULUT[1], Züleyha AKKAN ÇETİNKAYA[2], Mesut SEZİKLİ[1], Bülent YAŞAR[1], Selvinaz ÖZKARA[3], Ayşe Oya KURDAŞ ÖVÜNÇ[1]

Departments of [1]Gastroenterology and [3]Pathology Haydarpaşa Numune Education and Research Hospital, İstanbul
Department of [2]Gastroenterology, Kocaeli Derince Education and Research Hospital, Kocaeli

Background/aims: *The aim of this study was to evaluate the diagnostic accuracy of aspartate aminotransferase-platelet ratio index, the Forns index and FIB-4 for the assessment of hepatic fibrosis in chronic hepatitis C patients by comparison with liver biopsy.* ***Methods:*** *We retrospectively reviewed our computerized data of chronic hepatitis C patients who admitted to the Gastroenterology Clinic between 2004 and 2008. Treatment-naive chronic hepatitis C patients who had undergone liver biopsy and had laboratory test results allowing the calculation of aspartate aminotransferase-platelet ratio index, the Forns index and FIB-4 were included in this study. The degree of fibrosis was scored according to the METAVIR staging system. Significant fibrosis was defined as F2-4 and cirrhosis as F4. Aspartate aminotransferase-platelet ratio index, the Forns index and FIB-4 were calculated based on the original studies. Tests results were compared between groups F0-1 (no or mild fibrosis) versus F2-4 (significant fibrosis) and F0-3 (no cirrhosis) versus F4 (cirrhosis).* ***Results:*** *One hundred and fifty patients with chronic hepatitis C were included in this study. The areas under the ROC curves of the Forns index, aspartate aminotransferase-platelet ratio index and FIB-4 to predict significant fibrosis were 0.795, 0.774 and 0.764, respectively. The area under the ROC curves of the Forns index, aspartate aminotransferase-platelet ratio index and FIB-4 to predict cirrhosis were 0.879, 0.839 and 0.874, respectively.* ***Conclusions:*** *The Forns index, aspartate aminotransferase-platelet ratio index and FIB-4 were accurate noninvasive blood tests to predict the presence or absence of significant fibrosis and cirrhosis in half of the chronic hepatitis C patients. The Forns index was slightly better than the aspartate aminotransferase-platelet ratio index and FIB-4 in the prediction of significant fibrosis and cirrhosis.*

Key words: Chronic hepatitis C, fibrosis, AST-platelet ratio index (APRI), Forns index, FIB-4

Kronik hepatit C'li hastalarda belirgin fibrozis ve sirozun belirlenmesinde AST-platelet oranı indeksi, Forns indeksi ve FIB-4'ün yeri

Amaç: *Bu çalışmadaki amacımız kronik hepatit C'li hastalarda belirgin fibrozis ve sirozun belirlenmesinde aspartat aminotransferaz-platelet oranı indeksi, Forns indeksi ve FIB-4'ün tanısal güvenilirliğini karaciğer biopsisi ile karşılaştırmalı olarak değerlendirmektir.* ***Metod:*** *2004-2008 yılları arasında Gastroenteroloji Kliniği'ne başvuran kronik hepatit C'li hastaların bilgisayar kayıtlarını retrospektif olarak incelendi. Karaciğer biopsisi yapılmış ve aspartat aminotransferaz-platelet oranı indeksi, Forns indeksi ve FIB-4'ün hesaplanmasına olanak sağlayan laboratuvar test sonuçları olan hiç tedavi görmemiş kronik hepatit C'li hastalar çalışmaya alındı. Fibrozisin derecesi METAVIR sistemine göre belirlendi. F2-4 belirgin fibrozis, F4 siroz olarak kabul edildi. Aspartat aminotransferaz-platelet oranı indeksi, Forns indeksi ve FIB-4 orijinal çalışmalar esas alınarak hesaplandı. Test sonuçları hafif fibrozis ile belirgin fibrozisi olan gruplar ve sirozu olmayanlarla sirozu olan gruplar arasında karşılaştırıldı.* ***Bulgular:*** *150 kronik hepatit C'li hasta çalışmaya alındı. Belirgin fibrozisin belirlenmesinde Forns indeksi, aspartat aminotransferaz-platelet oranı indeksi ve FIB-4 için ROC eğrisi altında kalan alan sırası ile 0,795, 0,774 ve 0,764 idi. Sirozun belirlenmesinde Forns indeksi, aspartat aminotransferaz-platelet oranı indeksi ve FIB-4 için ROC eğrisi altında kalan alan sırası ile 0,879, 0,839 ve 0,874 idi.* ***Sonuç:*** *Forns indeksi, aspartat aminotransferaz-platelet oranı indeksi ve FIB-4, kronik hepatit C'li hastaların yarısında belirgin fibrozis ve sirozun belirlenmesinde güvenilir noninvaziv testlerdir. Hem belirgin fibrozis hem de sirozun belirlenmesinde Forns indeksi aspartat aminotransferaz-platelet oranı indeksine ve FIB-4'e göre hafif daha üstündür.*

Anahtar kelimeler: Kronik hepatit C, fibrozis, APRI, Forns indeksi, FIB-4

Address for correspondence: Fatih GÜZELBULUT
Haydarpaşa Numune Education and Research Hospital,
Gastroenterology, İstanbul, Turkey
E-mail: fguzelbulut@hotmail.com

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INTRODUCTION

Chronic hepatitis C virus (HCV) infection is a major public health problem (1,2). It is estimated that 180 million people worldwide are chronically infected with HCV (1). Chronic HCV infection is the major cause of chronic liver disease, cirrhosis and hepatocellular carcinoma in developed countries (1,3,4). Cirrhosis from chronic HCV infection is also the most common indication for liver transplantation (1,5).

Estimation of the prognosis and deciding on antiviral therapy for chronic HCV infection depend on the degree of hepatic fibrosis (2-6). Because the risk of cirrhosis development is low in patients with no or mild fibrosis, antiviral therapy may be delayed or withheld in these patients. On the other hand, patients with moderate to severe fibrosis must be treated, if there is no contraindication for therapy, as the development of cirrhosis is more likely in this group (3,7). The prediction of the cirrhosis is also important, since the presence of cirrhosis requires surveillance for hepatocellular carcinoma and portal hypertension (7,8).

Liver biopsy is the gold standard method for the assessment of hepatic fibrosis. However, it has some limitations. It is an invasive procedure and has serious complications in 0.5% of patients including even death (3,4,6,9-13). It cannot be performed in patients with impaired hemostasis (11,13). Since the biopsy specimens represent 1/50,000 of the liver, it can lead to under- or overestimation of the degree of hepatic fibrosis (6,7,13,14). Inter- and intraobserver discrepancies of 10% to 20% are other limitations (3,6,7,10,14). It is also costly (4,10,14,15).

In an attempt to overcome these limitations, several noninvasive tests, such as aspartate aminotransferase (AST)-to-platelet ratio index (APRI) (7), the Forns index (12), FIB-4 (15,16), Fibroindex (14), Fibrotest (17), Fibrometer (18), and Hepascore (19) have been developed to assess hepatic fibrosis. However, some of these tests require blood tests that are not part of the routine evaluation of patients with chronic hepatitis C (CHC). The main advantage of APRI, the Forns index and FIB-4 over other noninvasive tests is that they are based on readily available blood tests and are thus costless.

The Forns index is based on platelet count, gamma glutamyl transpeptidase (GGT), age, and cholesterol. The presence of significant fibrosis was predicted with a 96% negative predictive value (NPV) and 66% positive predictive value (PPV) (12).

The APRI is simple to use and is based on AST and platelet count. An 86% NPV and an 88% PPV were reported to predict the presence of significant fibrosis and a 98% NPV and a 57% PPV were reported to predict the presence of cirrhosis (7).

The FIB-4 was originally developed to predict significant fibrosis and cirrhosis among human immunodeficiency virus (HIV)/HCV coinfected patients in the APRICOT study (16). The test is based on AST, alanine aminotransferase (ALT), age, and platelet count. Subsequently, it was validated for HCV monoinfected patients by Vallet-Pichard et al. (15). In that study, using the cut-off values ≤1.45 and ≥3.25, an NPV of 94.7% and a PPV of 82.1% were reported to predict the presence of advanced fibrosis (15). A greater proportion of patients fell outside the cut-off ranges in both studies when compared with the APRI and Forns indices (7,12,15).

In the present study, we aimed to evaluate the diagnostic accuracy of APRI, the Forns index and FIB-4 for the assessment of hepatic fibrosis in chronic HCV monoinfected patients by comparison with liver biopsy.

MATERIALS AND METHODS

We retrospectively reviewed our computerized data of HCV monoinfected patients who admitted to the Gastroenterology Clinic between 2004 and 2008. One hundred and fifty consecutive HCV monoinfected patients with the following criteria were included in this study: 1) anti HCV and HCV RNA positivity, 2) liver biopsy prior to antiviral therapy or any other antifibrotic therapy, 3) laboratory test results allowing the calculation of APRI, the Forns index and FIB-4 obtained within 3 months from the date of liver biopsy, 4) absence of HIV and/or HBV coinfection, 5) absence of other liver diseases, 6) absence of hepatocellular carcinoma, 7) absence of prior liver transplantation, and 8) abstinence from alcohol abuse for more than 6 months.

All liver biopsy specimens were analyzed by a single pathologist. The degree of fibrosis was scored according to the METAVIR system, and no fibrosis was defined as F0, mild fibrosis as F1, moderate fibrosis as F2, severe fibrosis as F3, and cirrhosis as F4. Significant fibrosis was also defined as F2-4.

Laboratory test results, including AST, ALT, GGT, cholesterol, and platelet count, were collected. Age of the patient was age at the time of liver biopsy. We calculated APRI, the Forns index and FIB-4 based on the following formulas:

APRI = (AST/upper limit of normal [ULN])/platelet x 100;

Forns index = 7.811 – 3.131 x ln platelet + 0.781 x ln GGT + 3.647 x ln age – 0.014 x cholesterol;

FIB-4 = (age x AST)/(platelet x $ALT^{1/2}$).

We compared the APRI, Forns index and FIB-4 between the groups F0-1 (no or mild fibrosis) vs F2-4 (significant fibrosis) and F0-3 (no cirrhosis) vs F4 (cirrhosis). Statistical analysis was made using NCSS (Number Cruncher Statistical System) 2007 and PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA). Quantitative variables were presented as means (±SD), standard deviation, median, counts, and percentages. Student t test and Mann-Whitney U test were performed when comparing the quantitative variables between the groups. The diagnostic values of tests were compared by the area under the receiver operating characteristic (AUROC) curve and their corresponding 95% confidence intervals (CI). The diagnostic performance of each test was calculated according to PPV, NPV, sensitivity, and specificity. A p value <0.05 was considered as statistically significant. The present study was approved by the local ethics committee. Written informed consent was obtained from patients.

Table 1. Main characteristics of patients

	Mean ± SD (median)
Age (Mean SD)	52.37±10.80
Sex (Male) (%)	78 (52%)
Cholesterol	157.65±31.63
Platelet	196±77.29
AST (IU/ml)	63.56±46.78 (47)
ALT (IU/ml)	79.65±58.51 (64)
GGT (IU/ml)	69.08±65.47 (52)
AST/ULN	1.96±1.40 (1.44)
ALT/ULN	1.85±1.37 (1.47)
GGT/ULN	1.67±1.53 (1.47)
Fibrosis	
F0	33
F1	34
F2	23
F3	9
F4	51

AST: Aspartate aminotransferase. ALT: Alanine aminotransferase. GGT: Gamma glutamyl transpeptidase. ULN: Upper limit of normal.

RESULTS

One hundred and fifty patients with CHC were included in this study. All patients were white and 52% were male (n=78), with a mean age of 52.37±10.84 years. Eighty-three (55.3%) patients had significant fibrosis (F2-4) and 51 (34%) had cirrhosis (F4). The main characteristics of patients according to the fibrosis scores are shown in Table 1.

Mean age, cholesterol, platelet count, AST, ALT, GGT, Forns index, APRI, and FIB-4 in patients with no-mild fibrosis (F0-1) vs significant fibrosis (F2-4) and with no cirrhosis (F0-3) vs cirrhosis (F4) are shown in Table 2.

Prediction of Significant Fibrosis

ROC curves of the tests in the prediction of significant fibrosis are plotted in Figure 1. The AUROC curves of the Forns index, APRI and FIB-4 to predict significant fibrosis (F2-4) were 0.795, 0.774 and 0.764, respectively (Table 3).

For patients with a Forns score <4.2, 23 of 28 did

Table 2. Comparison of variables associated with the presence of significant fibrosis and cirrhosis

	Significant fibrosis			Cirrhosis		
	F0-1 (n=67) Mean±SD (median)	F2-4 (n=83) Mean±SD (median)	p	F0-3 (n=99) Mean±SD (median)	F4 (n=51) Mean±SD (median)	p
Age++	48.94±10.89	55.14±10.02	0.001**	49.65±10.94	57.67±8.47	0.001**
Cholesterol++	162.93±26.80	153.39±34.79	0.06	161.46±30.29	150.23±33.43	0.040*
Platelet++	224.48±64.86	173.02±79.65	0.001**	218.97±62.7	151.4±84.5	0.001**
AST+	47.28±31.94 (38)	76.69±52.82 (64)	0.001**	50.46±32.64 (40)	88.98±58.96 (71)	0.001**
ALT+	67.01±59.51 (49)	89.85±56.34 (73)	0.001**	70.46±55.06 (51)	97.49±61.92 (73)	0.001**
GGT+	49.31±54.31 (32)	85.03±69.92 (66)	0.001**	56.76±62.52 (37)	92.98±65.68 (75)	0.001**
Forns index	4.89±1.51 (5.05)	6.96±1.85 (6.88)	0.001**	5.13±1.49 (5.16)	7.78±1.67 (7.99)	0.001**
APRI	0.69±0.48 (0.54)	1.73±1.47 (1.26)	0.001**	0.77±0.56 (0.56)	2.22±1.61 (1.78)	0.001**
FIB-4	1.44±0.78 (1.34)	3.25±2.36 (2.57)	0.001**	1.55±0.91 (1.34)	4.18±2.48 (3.61)	0.001**

++Student t test *+Mann-Whitney U test* **p<0.05* ***p<0.01*

AST: Aspartate aminotransferase ALT: Alanine aminotransferase GGT: Gamma glutamyl transpeptidase APRI: AST-to platelet ratio index SD: Standart deviation

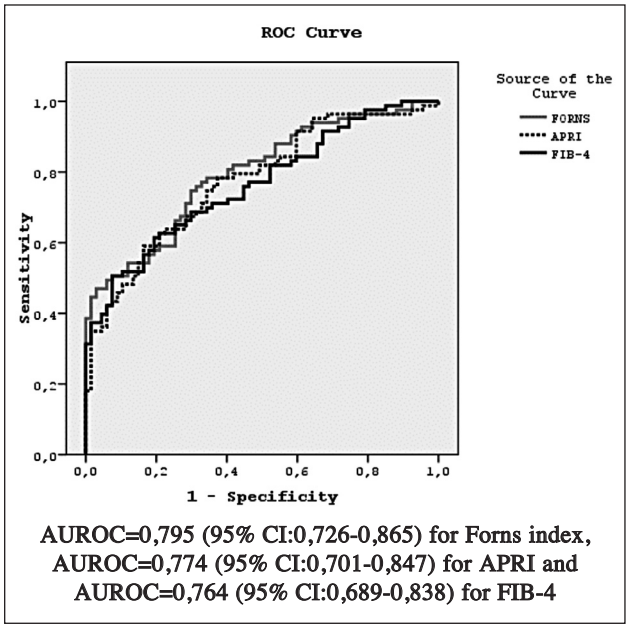

Figure 1. ROC curves of tests in the prediction of significant fibrosis

not have significant fibrosis, and for those with a Forns score >6.9, 39 of 43 had significant fibrosis.

Table 3. AUROC of fibrosis tests in the prediction of significant fibrosis and cirrhosis

	Significant fibrosis (F0-1 vs F2-4)		Cirrhosis (F0-3 vs F4)	
Test	Area	95% CI	Area	95% CI
Forns	0.795	0.726-0.865	0.879	0.818-0.940
APRI	0.774	0.701-0.847	0.839	0.770-0.908
FIB-4	0.764	0.689-0.838	0.874	0.817-0.932

CI: Confidence intervals APRI: AST-to-platelet ratio index

A Forns score <4.2 excluded significant fibrosis in 82.1% (NPV) of patients, with a sensitivity of 93.98%, and a Forns score >6.9 predicted significant fibrosis in 90.7% (PPV) of patients, with a specificity of 94.0% in 47.3% of patients.

For patients with an APRI of ≤0.5, 30 of 43 did not have significant fibrosis, and for those with an APRI of >1.5, 36 of 42 had significant fibrosis. An APRI ≤0.5 excluded significant fibrosis in 69.8% (NPV) of patients, with a sensitivity of 84.3%, and an APRI >1.5 predicted significant fibrosis in 85.7% (PPV) of patients, with a specificity of 91.0% in 56.7% of patients.

For patients with a FIB-4 of ≤0.6, all of 7 did not have significant fibrosis, and for those with a FIB-4 of ≥1, 76 of 123 had significant fibrosis. A FIB-4 ≤0.6 excluded significant fibrosis in 100% (NPV) of patients, with a sensitivity of 100%, and a FIB-4 ≥1 predicted significant fibrosis in 61.8% (PPV) of patients, with a specificity of 29.9% in 86.7% of patients.

Diagnostic accuracy of the tests in the prediction of significant fibrosis is shown in Table 4.

Prediction of Cirrhosis

ROC curves of the tests in the prediction of cirrhosis are plotted in Figure 2. The AUROC curves of the Forns index, APRI and FIB-4 to predict cirrhosis (F4) were 0.879, 0.839 and 0.874, respectively (Table 3).

For patients with a Forns score <4.2, 27 of 28 did not have cirrhosis, and for those with a Forns score >6.9, 34 of 43 had cirrhosis. A Forns score <4.2

Table 4. Diagnostic accuracy of tests in the prediction of significant fibrosis (F2-4)

			Fibrosis					
		Total (n)	0-1 (n=67) (44.7%)	2-4 (n=83) (55.3%)	Sen (%)	Spe (%)	PPV (%)	NPV (%)
APRI	**≤ 0.5**	43	30	13	84.34	44.78	65.42	69.77
	>0.5	107	37	70				
	≤ 1.5	108	61	47	43.37	91.04	85.71	56.48
	>1.5	42	6	36				
FIB-4	**≤0.6**	7	7	0	100	10.45	58.04	100
	>0.6	143	60	83				
	<1	27	20	7	91.57	29.85	61.79	74.07
	≥1	123	47	76				
Forns index	**<4.2**	28	23	5	93.98	34.33	63.93	82.14
	>4.2	122	44	78				
	<6.9	107	63	44	46.99	94.03	90.69	58.58
	>6.9	43	4	39				

Sen: Sensitivity. Spe: Specificity. PPV: Positive predictive value. NPV: Negative predictive value. APRI: AST-to-platelet ratio index.

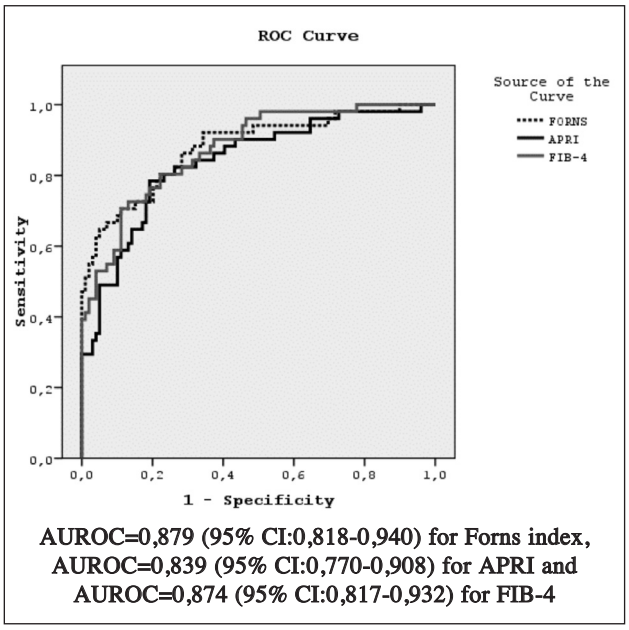

Figure 2. ROC curves of tests in the prediction of cirrhosis (F4)

excluded cirrhosis in 96.4% (NPV) of patients, with a sensitivity of 98.0%, and a Forns score >6.9 predicted cirrhosis in 79.1% (PPV) of patients, with a specificity of 90.9% in 47.3% of patients.

For patients with an APRI of ≤1, 80 of 94 did not have cirrhosis, and for those with an APRI of >2, 22 of 27 had cirrhosis. An APRI ≤1 excluded cirrhosis in 85.1% (NPV) of patients, with a sensitivity of 72.6%, and an APRI >2 predicted cirrhosis in 81.5% (PPV) of patients, with a specificity of 94.95% in 80.7% of patients.

For patients with a FIB-4 of ≤1.45, 57 of 62 did not have cirrhosis, and for those with a FIB-4 of ≥3.25, 28 of 36 had cirrhosis. A FIB-4 ≤1.45 excluded cirrhosis in 91.9% (NPV) of patients, with a sensitivity of 90.2%, and a FIB-4 ≥3.3 predicted cirrhosis in 77.8% (PPV) of patients, with a specificity of 91.9% in 65.3% of patients.

Diagnostic accuracy of the tests in the prediction of cirrhosis is shown in Table 5.

DISCUSSION

Assessment of the degree of hepatic fibrosis is essential in deciding on antiviral therapy for chronic HCV infection (2-6). Although liver biopsy remains the gold standard method for the assessment of hepatic fibrosis, it has some limitations (3,4,6,7,10-15). In order to overcome these limitations, several noninvasive blood tests, such as APRI (7), the Forns index (12), FIB-4 (15,16), Fibroindex (14), Fibrotest (17), Fibrometer (18), and Hepascore (19), have been developed to predict hepatic fibrosis. However, some of these tests require blood tests that are not part of the routine evaluation of patients with CHC.

In the present study, we aimed to evaluate the diagnostic values of the Forns index, APRI and FIB-4 to predict significant fibrosis and cirrhosis in our CHC patient cohort because these tests are combinations of readily available blood tests. We used the cut-off values based on the original studies (7,12,15,16).

The AUROC curves of the three tests were similar

Table 5. Diagnostic accuracy of fibrosis tests in the prediction of cirrhosis (F4)

			Fibrosis					
		Total	0-3 (n=99) (66%)	4 (n=51) (31%)	Sen (%)	Spe (%)	PPV (%)	NPV (%)
APRI	**≤ 1**	94	80	14	72.55	80.81	66.07	85.11
	>1	56	19	37				
	≤ 2	123	94	29	43.14	94.95	81.48	76.42
	>2	27	5	22				
FIB-4	**≤1.45**	62	57	5	90.20	57.58	52.27	91.94
	>1.45	88	42	46				
	<3.25	114	91	23	54.90	91.92	77.78	79.82
	≥ 3.25	36	8	28				
Forns index	**<4.2**	28	27	1	98.04	27.27	40.98	96.43
	>4.2	122	72	50				
	<6.9	107	90	17	66.67	90.91	79.07	84.11
	>6.9	43	9	34				

Sen: Sensitivity. Spe: Specificity. PPV: Positive predictive value. NPV: Negative predictive value. APRI: AST-to-platelet ratio index.

in the prediction of significant fibrosis and cirrhosis. As measured by the AUROC, all tests were better in the prediction of cirrhosis versus significant fibrosis. However, NPV and PPV varied between tests. The Forns index was slightly better than APRI in the prediction of significant fibrosis, with a higher PPV, NPV, sensitivity, and specificity. FIB-4 was excellent in the prediction of the absence of significant fibrosis, but it was poor in the prediction of the presence of significant fibrosis. The proportion of patients outside the cut-off values was higher with FIB-4 than with APRI and the Forns index.

On the other hand, all tests were similar in the prediction of the presence of cirrhosis. However, the Forns index predicted the absence of cirrhosis slightly better than APRI and FIB-4. However, the Forns index identified a lower proportion of patients than did the APRI and FIB-4.

The AUROC of each test was lower than those found in the original studies. The PPV and NPV of these tests were also different from the original studies (7,12,15,16). In Forns et al.'s study (12), NPV of the test was higher than PPV in the prediction of significant fibrosis. In contrast, our study yielded a slightly higher PPV. This may be due in part to the higher proportion of patients with significant fibrosis, since diagnostic performance of noninvasive tests varies according to the prevalence of significant fibrosis (3,12,20,21). The higher mean age of patients in our study may also have contributed to these different results (21). The AUROC of the Forns index in our study was similar to other studies in that the proportion of patients with significant fibrosis was higher (8,20,22,23). Koda et al. (14) also found results similar to ours, but they used different cut-off values. In addition to Forns et al., we also evaluated the Forns index in the prediction of cirrhosis using the same cut-off values. The Forns index was better in the prediction of the absence of cirrhosis than in the prediction of the presence of cirrhosis. The AUROC of the Forns index in the prediction of cirrhosis was also similar to Adler et al.'s study (23) and better than Leroy et al.'s study (8). Leroy et al. compared the Forns index in the prediction of advanced fibrosis (F3-4), but the proportion of our patients with F3 fibrosis was very low (8).

The PPV of the APRI was better than NPV in the prediction of significant fibrosis, similar to the results in Wai et al.'s study (7). In the prediction of cirrhosis, NPV of the APRI was higher than PPV, with a lower sensitivity and a higher specificity. However, the proportion of our patients with significant fibrosis and cirrhosis was higher than in Wai et al.'s study, and fibrosis was staged with the Ishak score in the original study, which may not truly overlap with METAVIR staging (7). Previous studies that evaluated the diagnostic performance of the APRI in the prediction of significant fibrosis and cirrhosis also showed different results (2,3,7). In our study, the AUROC of the APRI in the prediction of significant fibrosis was higher than in Cheung et al.'s study (5). In contrast to Silva et al.'s (3) study, in which the AUROC of APRI was 0.92 in the prediction of both significant fibrosis and cirrhosis, the APRI worked better in the prediction of cirrhosis than in the prediction of significant fibrosis. In contrast to a recently published metaanalysis by Shaheen et al. (2), APRI worked better in the prediction of significant fibrosis versus in the exclusion of significant fibrosis.

The AUROC of FIB-4 in the prediction of significant fibrosis was higher than that of Sterling et al.'s study (16). However, it should be kept in mind that FIB-4 was originally developed in HCV/HIV coinfected patients in whom ALT levels are known to be lower than in HCV monoinfected patients (24). Thus, higher ALT levels might lead to lower FIB-4 scores in HCV monoinfected patients. Another explanation of this result may be that fibrosis was staged with Ishak score in the original study (16). Vallet-Pichard (15) evaluated FIB-4 in HCV monoinfected patients in the prediction of severe fibrosis (METAVIR F3-4), and showed better AUROC than the original study as well as better NPV, with higher sensitivity and specificity. The AUROC of FIB-4 in our study was also similar to that study, although the proportion of patients with cirrhosis was higher in our study (15). In contrast to Adler et al.'s study (23), the Forns index was more useful than FIB-4 in the prediction of both significant fibrosis and cirrhosis.

The present study has some limitations. The normal range of AST, ALT, GGT, cholesterol, and platelet count vary according to the analyzers from various manufacturers between laboratories (3,5,14). Since the present study is retrospective, the levels of these tests were affected from time to time depending on the analyzer machine and method used (3,5,14). Thus, FIB-4 and the Forns index varied according to the analyzer machine used to measure the levels of these variables. On the other hand, APRI is a combination of the ratio of

AST/ULN and is partially corrected. However, this is a limitation not only of our study but also of the tests.

Cholesterol synthesis is affected not only by the severity of liver disease but also by several diseases, higher body mass index (BMI) and HCV genotype (12,22). As previously reported, higher serum GGT levels indicate the presence of hepatosteatosis and bile duct damage (12,25). Alcohol consumption and hepatosteatosis may lead to higher serum GGT levels (14). All these factors reduce the strength of the Forns index. We did not take into account the BMI of patients or alcohol consumption, since this study was retrospective and we did not have data about these variables. Progression of fibrosis correlates with duration of infection rather than the age of the patient (12), which might reduce the strength of the Forns index and FIB-4.

In conclusion, the Forns index, APRI and FIB-4 were accurate noninvasive blood tests to predict the presence or absence of significant fibrosis and cirrhosis in half of the patients. Although they were similar in accuracy, the Forns index was slightly better than APRI and FIB-4 in the prediction of both significant fibrosis and cirrhosis. The main advantage of these tests is that they are easily reproducible with readily available blood tests. The use of the combination of these tests may avoid the need for liver biopsy.

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