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AST-platelet ratio index cannot be used in the exclusion of significant fibrosis in chronic hepatitis B patients

To the Editor,

Guzelbulut et al. (1) demonstrated that the aspartate aminotransferase (AST)-platelet ratio index (APRI) may be a useful noninvasive marker in the exclusion of both significant fibrosis and cirrhosis because of the high negative predictive values (NPVs) in chronic hepatitis B (CHB). However, the NPVs for significant fibrosis and cirrhosis were 68% and 86%, respectively, for the same thresholds of the APRI in a recent meta-analysis (2). Because of this discrepancy, we retrospectively reviewed 229 CHB patients (142 males, 87 females) who had been followed up between 2009 and 2011 at our clinic.

The patients were aged between 18 and 75 years (mean 43.2±13.7) and met the following criteria: (1) HBsAg positivity 6 months longer, (2) blood test results for the assessment of APRI, (3) pre-treatment liver biopsy, (4) HBV-DNA ≥10,000 copies/mL, (5) absence of coinfection, and (6) absence of autoimmune hepatitis, hepatocellular carcinoma, and alcohol abuse. The Ishak system was used for the degree of fibrosis (3). Fibrosis was classified as no-mild fibrosis F0-2, significant fibrosis F3-6, and cirrhosis F5-6.

The area under the receiver operating characteristic curve (AUROC) values of the APRI to predict significant fibrosis and cirrhosis were 0.721 (95% CI, 0.655-0.787) and 0.720 (95% CI, 0.632-0.809), respectively. An APRI threshold of 0.5 was 91% sensitive and 29% specific at a 51.1% prevalence of significant fibrosis; this threshold had an NPV of 75%. With regard to cirrhosis, a threshold of 1.0 was 67% sensitive and 68% specific at a 15.7% prevalence of cirrhosis; the NPV of this threshold was 92% (Table 1).

AST-platelet ratio index was first reported by Wai et al. to determine patients with hepatitis C-related fibrosis in 2003 (4). Since then, a few studies have been done to evaluate the APRI for predicting fibrosis stage in CHB patients. But, some of the studies are debatable. In the study of Guzelbulut et al. (1), the AUROC values of APRI to predict significant fibrosis and cirrhosis were 0.779 and 0.781, and the NPVs for significant fibrosis and cirrhosis were 91% (APRI ≤0.5) and 92% (APRI ≤1), respectively. Similarly, our analysis suggests that APRI has limited value in identifying hepatitis B-related significant fibrosis and cirrhosis. But, we found a much lower NPV for significant fibrosis, consistent with the meta-analysis

Table 1. Diagnostic accuracy of APRI in the prediction of significant fibrosis and cirrhosis

			Fibrosis (n)		Sensitivity	Specificity	PPV	NPV
		Total	0-2	3-6	(%)	(%)	(%)	(%)
APRI	≤0.5	44	33	11				
	>0.5	185	79	106	90.6	29.4	57.3	75
	≤1.5	172	101	71				
	>1.5	57	11	46	39.3	90.2	80.7	58.7
			Fibrosis (n)		Sensitivity	Specificity	PPV	NPV
		Total	0-4	5-6	(%)	(%)	(%)	(%)
APRI	≤1	143	131	12	66.7	67.9	27.9	91.6
	>1	86	62	24				
	≤2	193	168	25	30.6	87.1	30.6	87.1
	>2	36	25	11				

PPV: positive predictive value; NPV: negative predictive value; APRI: AST-platelet ratio index

of Jin et al. (2). Thus, we think that APRI may be a useful noninvasive marker in the exclusion of cirrhosis in CHB patients. But, it can not be used in the exclusion of significant fibrosis.

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Author's Reply

To the Editor,

Thanks to the authors for their interest in our study (1). We read the meta-analysis by Jin et al (2). According to the EASL and AASLD guidelines, treatment desicion in chronic hepatitis B depends on the degree of necroinflammation and fibrosis in the liver (3,4). In patients with HBV DNA ≥20,000 IU/mL and ALT above 2 times the upper limit of normal (ULN), therapy should be started without liver biopsy (3,4). On the other hand, patients with HBV DNA ≥2,000 IU/mL and persistently normal/mildly elevated ALT (1-2xULN) especially those above age 30-40 should have undergone liver biopsy and be treated only when liver biopsy shows moderate/severe necroinflammation or significant fibrosis (3,4). However, these latter patients usually have minimal changes (5). So, liver biopsy may be unnecessary in the majority of them.

We aimed to evaluate whether APRI may obviate the need for liver biopsy in CHB patients. Because liver biopsy cannot be performed repeatedly due to its invasiveness, cost and risks. In our study, NPVs for the exclusion of significant fibrosis and cirrhosis were 91% and 92%, respectively (1). In the study by Jin et al, using cut off values ≤0.5 and ≤1-1.5, significant fibrosis and cirhosis were excluded with NPVs of 68% and 86%, respectively (2). Using the same cut off values in their CHB patients, the authors of the letter reached similar results to Jin et al. In that analysis, significant fibrosis and cirrhosis were excluded with NPVs of 75% and 92%, respectively. NPV of the APRI for the exclusion of significant fibrosis was much higher in our study than other 2 analysis.

First, difference may result from characteristics of the patient groups. The prevalance of significant fibrosis was 26% in our study, while they were 53% and 51% in those analysis. Similar results between the studies with regard to cirrhosis supports this idea, because prevalance of cirrhosis are similar (15.6% vs 13.5%-15.7%) (1,2). Second, the course of CHB is different from chronic hepatitis C (CHC). Unlike CHC patients, CHB patients commonly experience acute flares with fluctuating transaminase levels which may lead to high APRI values despite low fibrosis scores during flares or low APRI scores despite high fibrosis scores between flares. Consistent with this idea, NPV of APRI ≤0.5 for the exclusion of significant in CHC was 70%, which was much lower than in CHB, in our another study (6).

In summary, APRI may be a useful marker in the exclusion of significant fibrosis in CHB. However, it should be kept in mind that the course of CHB may lead to false results. Different inclusion criteria may also lead to different results between studies.

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