

B

AST/

Efficacy of AST to Platelet Ratio Index in Predicting Severe Hepatic Fibrosis and Cirrhosis in Chronic Hepatitis B Virus Infection

Sung Jun Sim, M.D., Jae Youn Cheong, M.D., Sung Won Cho, M.D., Jong Su Kim, M.D., Tae Young Lim, M.D., Do Hyun Shin, M.D., Sun Gyo Lim, M.D., Young Bae Kim, M.D.*, Kee Myung Lee, M.D., Byung Moo Yoo, M.D., Kwang Jae Lee, M.D., Ki Baik Hahm, M.D., and Jin Hong Kim, M.D.

Departments of Gastroenterology and Pathology*, Genomic Research Center for Gastroenterology, Ajou University College of Medicine, Suwon, Korea

Background/Aims: An ideal noninvasive diagnostic test for hepatic fibrosis should be simple, inexpensive, and accurate. We aimed to find the simple marker for predicting hepatic fibrosis and to compare the accuracy of AST, platelet, AST/ALT ratio and AST to platelet ratio index (APRI) in chronic hepatitis B patients without clinical evidence of cirrhosis. Methods: A total of one hundred and twenty-six chronic hepatitis B patients who underwent liver biopsy at the Ajou University Hospital from August 1998 to December 2003 were enrolled. Hepatic fibrosis was assessed using the Ludwig classification. Significant fibrosis was defined as fibrosis score of 3 or more. The AST/ALT ratio and APRI were calculated and correlations with hepatic fibrosis were analyzed. Results: APRI showed a significant correlation (r=0.501, p=0.000) with hepatic fibrosis, and was superior to AST, AST/ALT ratio and platelet in predicting fibrosis. Patients with significant fibrosis (fibrosis stage 3, 4) can be identified to have APRI=1 with sensitivity 71.2% and specificity 70.3%. The sensitivity and specificity of an APRI = 1.5 for cirrhosis (stage 4) were 83.3% and 75.0%. Conclusions: Simple index using AST and platelet value can predict the presence of significant fibrosis and cirrhosis in chronic hepatitis B patients without clinical evidence of cirrhosis. (Korean J Gastroenterol 2005;45:340-347)

Key Words: Hepatitis B; Liver fibrosis; AST/ALT ratio; AST to platelet ratio index

: 2004 8 24 , : 2005 3 7
: , 442-821, 5

Tel: (031) 219-6939, Fax: (031) 219-5999
E-mail: jaeyoun2@dreamwiz.com

Correspondence to: Jae Youn Cheong, M.D.
Department of Gastroenterology, Ajou University College of Medicine
San 5 Woncheon-dong, Yeongtong-gu, Suwon 442-821, Korea
Tel: +82-31-219-6939, Fax: +82-31-219-5999
E-mail: jaeyoun2@dreamwiz.com

*

(01-PJ10-PG6-01GN14-0007).

B 126

B 가 73%, 20 g 77% .¹ 가 , anti-HCV 가

B 가 .^{2,3} 2.

가 , B 가 , 가 .⁴

가 . B 가 aminotransferase

ala- nine aminotransferase (ALT) aspartate aminotransferase (AST) , 5 mm hematoxylin-eosin Mas- son-trichrome Ludwig ,¹² 0

가 .⁵ 가 4, 1 4 , 3 4 가

가 .⁶⁻⁸ AST/ALT AST/ (AST to platelet ratio index, APRI) 3.

가 .^{9,10} C t-

AST/ALT Spearman SPSS 11.0 (SPSS Inc., Chicago, IL, USA) , p 0.05

가 B 가 AST, ALT, AST/ALT , AST/ ROC (receiver operating characteristic) curve , 가 cut-off

111 (88.1%), 15 (11.9%) .
 AST 132.1±178.3 IU/L, ALT 164.6±191.8 IU/L,
 1.1±1.3 mg/dL, 7.3±0.5 g/dL, 4.2
 ±0.4 g/dL, 88.3±26.3 IU/L, -FP 13.4±
 31.0 pg/mL , 191,547±55,358/mm³ .
 ()
 1 2) (3 4)
 , , , , , AST,
 ALT,
 , -FP
 ,
 1.5±0.5, 3.4±0.5 ,
 2.3±1.0 (Table 1).
 , 0 16 (12.7%), 1
 17 (13.5%), 2 31 (24.6%), 3 39 (31.0%), 4 23
 (18.3%) (Fig. 1), 1 38 (30.2%),
 2 36 (28.6%), 3 34 (27.0%), 4 18 (14.3%)
 (Fig. 2).

2. AST/ALT AST/

가

AST , AST/ALT , AST/
 . APRI

10

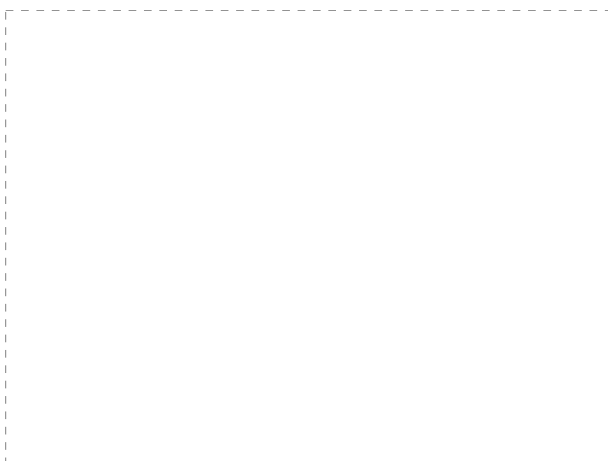


Fig. 1. Distribution of hepatitis activity grade.

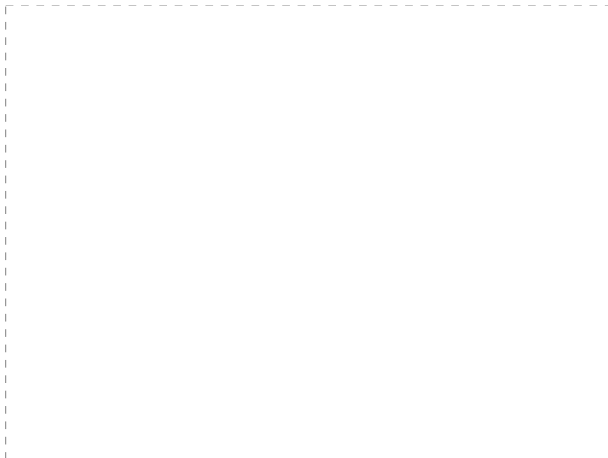


Fig. 2. Distribution of hepatic fibrosis stage.

Table 1. Baseline Characteristics of Patients

	No significant fibrosis (stage 1, 2)		Significant fibrosis (stage 3, 4)		p-value	Total	
	Mean±SD	n	Mean±SD	n		Mean±SD	n
Age (year)	25.3±8.5	74	32.6±8.7	52	0.000	28.3±9.2	126
Platelet (×10 ³ /mm ³)	214,013±50,415	74	159,576±45,809	52	0.000	191,547±55,358	126
Total bilirubin (mg/dL)	0.8±0.5	72	1.5±1.8	50	0.002	1.1±1.3	122
Total protein (g/dL)	7.3±0.4	69	7.3±0.6	47	0.997	7.3±0.5	116
Albumin (g/dL)	4.3±0.3	72	4.1±0.4	50	0.001	4.2±0.4	122
AST (U/L)	81.3±97.8	74	204.4±234.8	52	0.000	132.1±178.3	126
ALT (U/L)	108.3±112.2	74	244.8±247.0	52	0.000	164.6±191.8	126
ALP (IU/L)	83.7±24.4	68	94.6±27.7	49	0.026	88.3±26.3	117
AFP (ng/mL)	3.5±2.7	19	22.9±41.4	20	0.049	13.4±31.0	39
Fibrosis stage	1.5±0.5	74	3.4±0.5	52	0.000	2.3±1.0	126

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; AFP, alpha-fetoprotein.

APRI
$$= \frac{\text{AST level (/ULN)}}{\text{Platelet counts (10}^9\text{/L)}} \times 100$$

 (ULN: upper limit of normal)
 AST (r=0.424, p=0.000) APRI (r=0.501, p=0.000)
 (r=-0.492, p=0.000)
 (Table 2)(Fig. 3). AST/ALT
 (Table 2) (Fig. 4).

3. APRI cut off

APRI ROC curve cut-off
 (Table 3, 4)(Fig. 5). ROC curve APRI area
 under the curve (AUC) 0.794 AST/ALT
 가
 (Fig. 5).

4 APRI cut-off 1 1.5

52 APRI 1 15 (28.8%), 1 37
 (71.2%), APRI 1.5 22 (42.3%), 1.5
 30 (57.7%) (Table 3).
 APRI cut-off 1 71.2%,
 70.3%, 62.7%, 77.6% ,
 APRI cut-off 1.5 57.7%,
 83.8%, 71.4%, 73.3% (Table 4).

Table 2. Correlation of the Hepatic Fibrosis and AST, Platelet, AST/ALT Ratio and APRI

	Correlation coefficient	p
Spearman's rho	APRI 0.501	0.000
	AST/ALT ratio 0.004	0.963
	AST 0.424	0.000
	Platelet -0.492	0.000

APRI, AST to platelet ratio index.

Ludwig 4
 APRI 18 APRI 1
 1 (5.6%), 1 17 (94.4%) , APRI 1.5

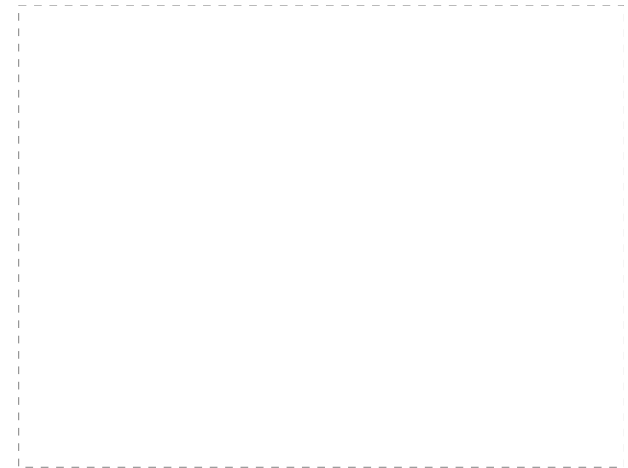


Fig. 3. Relationship of AST/ALT ratio and hepatic fibrosis stage. AST/ALT ratio showed no significant correlation with hepatic fibrosis (r=0.004, p=0.963).

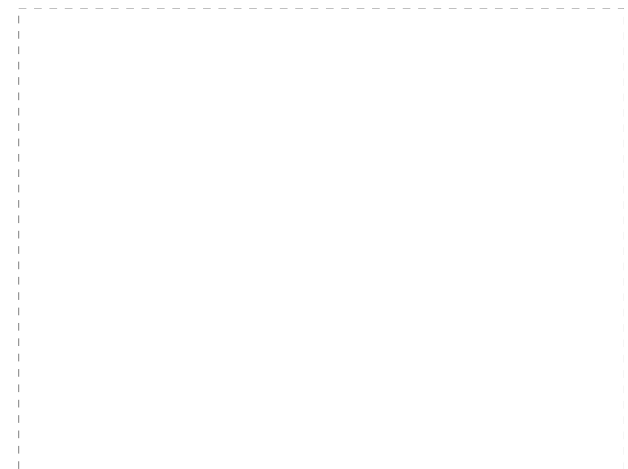


Fig. 4. Relationship of APRI and hepatic fibrosis stage. There is a significant correlation between APRI and hepatic fibrosis (r=0.501, p=0.000). APRI, AST to platelet ratio index.

Table 3. Distribution of Hepatic Fibrosis according to Different APRI Cuf-off Value

APRI cut-off	Stage 1, 2 (n=74)	Stage 3, 4 (n=52)	Stage 1, 2, 3 (n=108)	Stage 4 (n=18)
1	52 (70.3%)	15 (28.8%)	66 (61.1%)	1 (5.6%)
>1	22 (29.7%)	37 (71.2%)	42 (38.9%)	17 (94.4%)
1.5	62 (83.8%)	22 (42.3%)	81 (75.0%)	3 (16.7%)
>1.5	12 (16.2%)	30 (57.7%)	27 (25.0%)	15 (83.3%)

APRI, AST to platelet ratio index.

Table 4. Prediction of Hepatic Fibrosis by AST/ALT Ratio and Two APRI Cut-off Value

	APRI				AST/ALT ratio
	Stage 3, 4 (significant fibrosis)		Stage 4 (cirrhosis)		
Cut-off value	1	1.5	1	1.5	1
Sensitivity	71.2%	57.7%	94.4%	83.3%	57.1%
Specificity	70.3%	83.8%	61.1%	75.0%	59.5%
PPV	62.7%	71.4%	28.8%	35.7%	34.6%
NPV	77.6%	73.8%	98.5%	96.4%	67.6%

PPV, positive predictive value; NPV, negative predictive value; APRI, AST to platelet ratio index.

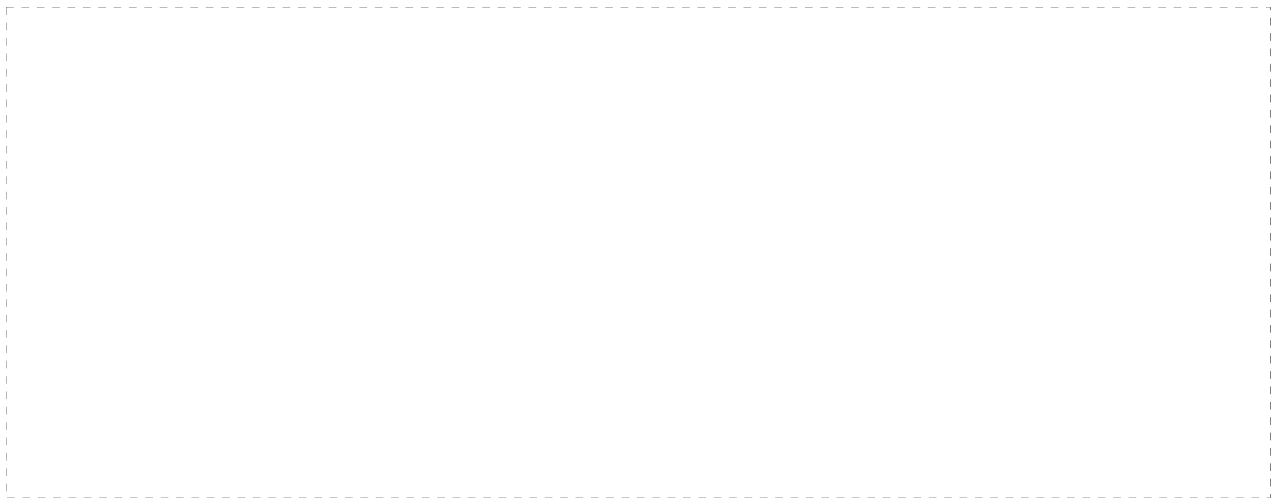


Fig. 5. ROC curve of the AST/ALT, APRI and platelet in predicting hepatic fibrosis. (A) Prediction of significant fibrosis (stage 3, 4). (B) Prediction of cirrhosis (stage 4). APRI, AST to platelet index.

3 (16.7%), 1.5 (83.3%) APRI ROC AUC 0.794
 (Table 3). APRI cut-off
 1 94.4%, 61.1%, 28.8%, AST/ALT 8,11 12
 98.5%, APRI cut-off 1.5
 83.3%, 75.0%, 35.7%, 96.4% APRI 1 가 ,
 (Table 4). 1.5
 AST/ALT Sheth 9 cut-off
 1
 57.1%, 59.5%, 34.6%, 13
 67.6% 가 .
 . 4
 B
 가 B ,
 . AST 6-8 가

가 .²²

B C 가 B AST/ALT

AST/ALT
(r=0.137),
(r=-0.343).

가 .⁵ AST/ALT
AST/ALT 1
150,000/mm³ 98.8%
가 8.5% AST

(r=0.424) ,
(r=-0.492) , APRI
(r=0.501).

AST/ALT APRI cut-off 1.5 75%, 83.3%

AST/ALT 가 1 가 AST

가 .¹⁶ AST ALT
가 , Child
AST ALT 가 가
가 .¹⁶ AST가 (hepatic sinusoidal
cell) 가 AST

ROC curve APRI cut-off 1 1.5

가 .^{17,18} AST ALT 4 , 1.5

ALT 가 .¹⁶ AST/
가 가

ALT .^{9,19,20} C AST/ALT 가
가 , AST/ALT

가 1 35% .²⁰ 가

AST ALT ALT , 가

AST ALT AST/
AST/ALT , AST/ 가 1

가 .²⁰ AST , 1.5
AST/
가

가 , AST/ALT
가

ALT ,
AST/ALT

가 가 가

.²¹ :

가 B
 가 AST, ALT,
 AST/ALT , AST/
 가
 : 1998 8
 2003 12 B
 126
 (3, 4)
 (4) Ludwig :
 AST/
 (r=0.501, p=0.000), AST
 . AST/ALT
 가 (r=0.004). AST/
 ROC curve
 cut-off
 APRI 1 71.2%, 70.3%,
 62.7%, 77.6% ,
 APRI 1.5 83.3%, 75.0%,
 35.7%, 96.4% . :
 가 B AST/

: B , AST/ALT , AST/ ,

1. Shin HS, Han KH, Park SJ, et al. The prevalence of hepatitis virus infection and clinical characteristics in patients with hepatocellular carcinoma. *Korean J Med* 1994;46:467-476.
2. Needleman L, Kurtz AB, Rifkin MD, Cooper HS, Pasto ME, Goldberg BB. Sonography of diffuse benign liver disease: accuracy of pattern recognition and grading. *AJR Am J Roentgenol* 1986;146:1011-1015.
3. Simonovsky V. The diagnosis of cirrhosis by high resolution ultrasound of the liver surface. *Br J Radiol* 1999;72:29-34.
4. Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies. *J Hepatol* 1986;2:165-173.
5. Aube C, Oberti F, Korali N, et al. Ultrasonographic diagnosis of hepatic fibrosis or cirrhosis. *J Hepatol* 1999;30:472-478.
6. Myers RP, Ratzu V, Imbert-Bismut F, Charlotte F, Poynard T. Biochemical markers of liver fibrosis: a comparison with historical features in patients with chronic hepatitis C. *Am J*

- Gastroenterol* 2002;97:2419-2425.
7. Wong VS, Hughes V, Trull A, Wight DG, Petrik J, Alexander GJ. Serum hyaluronic acid is a useful marker of liver fibrosis in chronic hepatitis C virus infection. *J Viral Hepat* 1998;5:187-192.
8. Imbert-Bismut F, Ratzu V, Pieroni L, Charlotte F, Benhamou Y, Poynard T. Biochemical markers of liver fibrosis in patients with hepatitis C virus infection: a prospective study. *Lancet* 2001;357:1069-1075.
9. Sheth SG, Flamm SL, Gordon FD, Chopra S. AST/ALT ratio predicts cirrhosis in patients with chronic hepatitis C virus infection. *Am J Gastroenterol* 1998;93:44-48.
10. Wai CT, Greenson JK, Fontana RJ, et al. A simple non-invasive index can predict both significant fibrosis and cirrhosis in patients with chronic hepatitis C. *Hepatology* 2003;38:518-526.
11. Park SY, Kang KH, Park JH, et al. Clinical efficacy of AST/ALT ratio and platelet counts as predictors of degree of fibrosis in HBV infected patients without clinically evident liver cirrhosis. *Korean J Gastroenterol* 2004;43:246-251.
12. Ludwig J. The nomenclature of chronic active hepatitis: an obituary. *Gastroenterology* 1993;105:274-278.
13. Brook MG, Karayiannis P, Thomas HC. Which patients with chronic hepatitis B virus infection will respond to alpha-interferon therapy? A statistical analysis of predictive factors. *Hepatology* 1989;10:761-763.
14. Correia JP, Alves PS, Camilo EA. SGOT-SGPT ratios. *Dig Dis Sci* 1981;26:284.
15. Nalpas B, Vassault A, Le Guillou A, et al. Serum activity of mitochondrial aspartate aminotransferase: a sensitive marker of alcoholism with or without alcoholic hepatitis. *Hepatology* 1984;4:893-896.
16. Williams AL, Hoofnagle JH. Ratio of serum aspartate to alanine aminotransferase in chronic hepatitis. Relationship to cirrhosis. *Gastroenterology* 1988;95:734-739.
17. Kamimoto Y, Horiuchi S, Tanase S, Morino Y. Plasma clearance of intravenously injected aspartate aminotransferase isozymes: evidence for preferential uptake by sinusoidal liver cells. *Hepatology* 1985;5:367-375.
18. Okuda M, Li K, Beard MR, et al. Mitochondrial injury, oxidative stress, and antioxidant gene expression are induced by hepatitis C virus core protein. *Gastroenterology* 2002;122:366-375.
19. Pohl A, Behling C, Oliver D, Kilani M, Monson P, Hassanein T. Serum aminotransferase levels and platelet counts as predictors of degree of fibrosis in chronic hepatitis C virus infection. *Am J Gastroenterol* 2001;96:3142-3146.

20. Reedy DW, Loo AT, Levine RA. AST/ALT ratio \geq 1 is not diagnostic of cirrhosis in patients with chronic hepatitis C. *Dig Dis Sci* 1998;43:2156-2159.
 21. Aster RH. Pooling of platelets in the spleen: role in the pathogenesis of "hypersplenic" thrombocytopenia. *J Clin Invest* 1966;45:645-657.
 22. Kawasaki T, Takeshita A, Souda K, et al. Serum thrombopoietin levels in patients with chronic hepatitis and liver cirrhosis. *Am J Gastroenterol* 1999;94:1918-1922.
-