The comparison of liver fibrosis score and non-invasive tests in naive chronic viral hepatitis B patients.

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Abstract

Background/aims: Chronic Viral Hepatitis B (CVHB) disease is a major health problem in our country and the world. Liver biopsy is still the gold standard today to show liver fibrosis and necro-inflammatory activity. Liver biopsy is an invasive procedure. Therefore, in recent years, the development of non-invasive and practical testing has gained importance to show liver fibrosis In this study, it was aimed to compare the results of APRI, AP index, FIB-4, AAR panel tests with the degree of liver fibrosis. Materials and methods: 150 naive CVHB patients who were conducted percutaneous liver biopsy examined retrospectively. The following non-invasive tests (APRI, APindex, FIB-4, AAR) were calculated and they were compared with the fibrosis score.

Results: It was statistically significant between an increase in FIB-4 score and an increase in the degree of fibrosis (P=0.03). FIB-4 values $\geq$ 3.25 and it was considered significant to show the disease. It was statistically significant between an increase in AP index score and an increase in the degree of fibrosis (P=0.015)

Conclusion: It is considered that non-invasive tests are quite useful in showing the status of liver fibrosis in patients with CVHB.

Introduction

Chronic Viral Hepatitis B (CVHB) disease is a major health problem in our country and in the world. In these patients, the most commonly used method is percutaneous liver biopsy to show the degree of fibrosis in the liver [1]. Liver biopsy is an invasive procedure, it has approximately 0.3-0.6% morbidity and 0.05% mortality risk and patients must be followed 6-18 h in hospital conditions after the procedure [2]. Needle biopsies smaller than 2 cm and containing less than 11-15 portal areas has been reported not to fully reflect the current situation of grade of hepatitis and stage of fibrosis [3]. In some studies comparing the histopathological method with biochemical markers, false negativities of the histopathological interpretations have been demonstrated [4]. Therefore, in recent years, the development of non-invasive and practical testing has gained importance to show liver fibrosis. In this study, it was aimed to compare the results of aspartat aminotransferaz to platelet ratio index (APRI), Age-Platelet index (AP index): Fibrosis-4 score (FIB-4), Aspartat aminotransferase (AST) to alanine aminotransferase (ALT) ratio (AAR) test panels with the degree of liver fibrosis reported histopathologically.

Materials and Methods

Percutaneous liver biopsies of naive 150 KVHB patients were performed in the department of gastroenterology and hepatology between 2011-2014 patients were analyzed retrospectively. The histopathological evaluation of the liver biopsies was performed according to the Modified Knodell Classification (Ishak) chronicity index score by the same pathology unit. 21 patients were excluded from the study due to fibrosis score has to be 0. 101 patients with fibrosis scores between 1-3 and 28 patients with scores between 4-6 were included in the study. The following non-invasive tests were calculated and they were compared with the fibrosis score. FIB-4 score: It was calculated with (Age × AST)/platelet value × ALT and FIB-4 score<1.45 shows no fibrosis and score FIB-4 score>3.25 shows significant fibrosis. The patients were included in two groups as FIB-4: <3.25 and $\geq$ 3.25.

APRI score: <0.5 shows no fibrosis and APRI score $\geq$ 1.5 shows significant fibrosis. The patients were included in two groups as APRI $\geq$ 1.5 and <1.5.

AP index: Patient ages<30: 0 point, ages between 30-39: 1 point, ages between 40-49 age: 2 points, ages between 50-59: 3 points, ages between 60-69: 4 points, ages $\geq$ 70: 5 points and platelet count: 340 × 10/L: 0 point, platelet count: 280-339 10/L: 1 point, platelet count: 220-279 10/L: 2 points, platelet count: 160-219 10/L: 3 points, platelet count: 100-159 10/L: 4

points, platelet count: 40-99 10/L: 5 points, platelet count: <40 10/L: 6 points) and if it is ≥ 6, it shows significant fibrosis and if it is <6, it shows no fibrosis. The patients were included in two groups as AP index ≥ 6 and <6.

AAR was calculated according to AST/ALT formula, it is estimated that AAR<1 shows mild fibrosis and AAR ≥ 1 shows significant fibrosis. The patients were included in two groups as AAR ≥ 1 and <1. It was statistically compared using the Mann-Whitney U test. The sensitivity, specificity, positive and negative predictive values four mentioned test in showing significant fibrosis was calculated with 95% confidence intervals. SPSS 17.0 was used as statistical package program in data analysis.

Results

Panel tests were compared in respect to specificity, sensitivity, positive predictive and negative predictive values between the degrees of fibrosis. If FIB-4 value is ≥ 3.25, specificity has increased from 75.0% to 97.22% but the sensitivity has not increased. There was a statistically significant correlation between an increase in FIB-4 score and an increase in the degree of fibrosis (p: 0.03). Moreover, while negative predictive value was high (1.30) in FIB-4 values<3.25 and it was considered significant to show healthy people, positive predictive value was 1.11 in FIB-4 values ≥ 3.25 and it was considered significant to show the disease. The specificity and sensitivity is low between APRI score<1.5 and fibrosis score and it was not found to be statistically significant (p: 0.68). It was not found to be statistically significant between APRI score<1.5 and fibrosis score (p: 0.88) (Table 1).

The specificity was high as 87% and the sensitivity was low between patients with AP index score<6 and patients with AP index score ≥ 6 and fibrosis score (29.8%). While positive predictive values were significantly high as (1.25), negative predictive values were observed as (0.4). There was statistically significant correlation between increase in AP index score and increase in the degree of fibrosis (p=0.015).

Table 1. Patient groups, the statistical results of non-invasive testing.

	Fibrosis 1-3, n: 101	Fibrosis 4-6, n:28	Specificity	Sensitivity	Positive predictive	Negative predictive	P
FIB-4 (<3.25)	60	50	0.75	0.4211	0.59	1.3	
FIB-4 (≥ 3.25)	7	12	0.9722	0.1228	1.11	0.23	p: 0.03
APRI<1.5	61	46	0.597	0.4386	1.06	0.9	p: 0.68
APRI ≥ 1.5	10	12	0.902	0.105	1.1	0.9	p: 0.88
API<6	63	40	0.875	0.298	1.25	0.4	p: 0.015
API ≥ 6	9	17					
AAR<1	65	27	0.791	0.2283	1.03	0.8	p: 0.78
AAR ≥ 1	18	19					

Abbreviations: FIB-4: Fibrosis-4 score; APRI: Aspartat Aminotransferaz Platelet Ratio Index; API: Age-Platelet Index; AAR: AST/ALT Ratio.

If the ratio of AAR was ≥ 1, while the specificity was 79.1%, the sensitivity was 22.8%, positive predictive value was 1.03, negative predictive value was 0.8 between the degrees of liver fibrosis and positive predictive value and negative predictive values were seen close to each other. There was no statistically significant relationship between AAR and the degree of fibrosis (Table 1).

Discussion

Liver biopsy is still the gold standard today to show liver fibrosis and necroinflammatory activity in CVHB patients [5,6]. Because it does not affect in the same way every region of the liver in CVHB, it is considered that a single biopsy sample does not always reflect the characteristics of the disease and the degree of fibrosis. Various scorings are used in histopathological examination. One of the most commonly used scores is Modified Knodell Classification (Table 2). The most commonly used non-invasive tests in showing liver fibrosis are based on measurements of serum levels of various molecules. An ideal non-invasive test to be used in showing fibrosis is able to obtain simply and easily, must be cheap and reliable. APRI, FIB-4 score, AP index, AAR tests are the most widely used among these [7]. In the study conducted by Zhang et al., a significant relationship has been detected between FIB-4 scores of 212 patients with CVHB and histologic features and they evaluated FIB-4 score as the major fibrous marker [3]. Similarly in our study, there was the relationship between FIB-4 score and the degree of liver fibrosis, if FIB-4 value is ≥ 3.25; the specificity has increased (Table 1). There was a statistically significant correlation between increase in FIB-4 score and increase in the degree of fibrosis (p: 0.03). In a study conducted by Yilmaz et al., while APRI score was compatible with fibrosis in patients with CVHC, it was not found to be compatible with fibrosis in CVHB [8]. In the study of Wai et al., they stated that APRI value can be used to predict fibrosis and cirrhosis [9]. However, in our study, there was no

statistically significant correlation between APRI score and the degree of fibrosis (Table 1).

Table 2. Modified Knodell Classification (Ishak), Chronicity index [6].

No fibrosis	0
Fibrous expansion of some portal areas with or without short fibrous septa:	1
Fibrous expansion of most portal areas with or without short fibrous septa:	2
Fibrous expansion of most portal areas with occasional portal-portal (P-P) bridging:	3
Fibrous expansion of portal areas with marked portal-portal (P-P) bridging and at the same time portal-central (P-C) bridging's	4
Marked (P-P) and (P-C) bridging's and occasional nodule formation:	5
Cirrhosis clearly or definitely available	6

Ma et al. found in study of 1168 CVHB patients with severe liver fibrosis that FIB-4 and AP index were correlated well with fibrosis [10]. In the study performed prospectively by Mahassadi et al. it has been shown that APRI, AAR, AP index and FIB-4 index are effective to determine significant fibrosis or cirrhosis in 117 patients with CVHB APRI, AAR, AP index, FIB-4 index and high FIB-4 score is an important distinguishing between severe fibrosis and mild to moderate fibrosis [11]. In the study of Giannini et al. in cases of CVHB, they have found that the most reliable tests were AP index, AAR test [12]. In study performed by Abdollahi et al. the high correlation has been shown between fibrosis score of liver biopsy and AAR, APRI, and FIB-4 tests in 281 patients with CVHB, in addition, FIB-4 and APRI were found to be more superior and high diagnostic accuracy than AAR in distinguishing mild to moderate fibrosis from severe fibrosis [13]. Similarly in our study, we found that AP index and FIB-4 score were more valuable tests than APRI and AAR. We did not detect a significant correlation between AAR and APRI tests (Table 1).

Result: It is considered that non-invasive tests are quite useful in showing the status of liver fibrosis in patients with CVHB the concomitant usage of these tests may be successful to varying degrees in showing fibrosis.

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