Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2021;46(3):1237-1244
DOI: 10.17826/cumj.899586

ARAŞTIRMA / RESEARCH

Relationship of hemogram and biochemical parameters with modified histologic activity index and hepatic fibrosis in chronic hepatitis B

Kronik hepatit B'de hemogram ve biyokimyasal parametrelerin modifiye histolojik aktivite indeksi ve hepatik fibrozis ile ilişkisi

Selma Erdoğan Düzcü[1], Şeyma Öztürk[1]

[1]Bolu Abant Izzet Baysal University Medical School, Department of Pathology, Bolu, Turkey

Cukurova Medical Journal 2021;46(3):1237-1244.

Abstract

Purpose: Chronic hepatitis B is still one of the leading causes of cirrhosis and hepatocellular carcinoma worldwide, and the liver biopsy the gold standard method to assess the severity of liver fibrosis. Noninvasive predictive factors are needed for histological evaluation of liver biopsies. In this study, it was aimed to investigate the diagnostic value of hemogram and biochemical parameters for modified histological activity index and fibrosis in patients with chronic hepatitis B.

Materials and Methods: In this study, liver tru-cut biopsies of 248 patients diagnosed with chronic hepatitis B, were evaluated retrospectively. Modified histological activity index and fibrosis were scored in accordance with the Ishak staging system and compared with hemogram and biochemical parameters.

Results: In the fibrosis groups, the aspartate aminotransferase (AST) value was the best marker to discriminate < 3 ve ≥3 groups, with 70,3% discrimination performance. In the histological activity index groups, AST, alanine aminotransferase (ALT), and gamma-glutamyl transferase (GGT) was the best parameters to discriminate <6 ve ≥6 groups with 75,5%, 73,7%, and 73,4% discrimination performances, respectively.

Conclusion: In our study, we showed that noninvasive parameters used in clinical practice in patients with chronic hepatitis B have diagnostic value in predicting fibrosis and necroinflammatory activity.

Keywords:. Chronic hepatitis B, histological activity index, liver fibrosis, complete blood count, biochemistry

Öz

Amaç: Kronik hepatit B sirozun ve hepatosellüler karsinomun önemli nedenlerinden biri olup karaciğer biopsisi fibrozis tanısında altın standart yöntemdir. Karaciğer biopsilerinin histolojik değerlendirilmesinde noninvaziv prediktif faktörlere ihtiyaç vardır. Bu çalışmada kronik hepatit B vakalarında modifiye histolojik aktivite indeksi ve fibrozis için hemogram ve biyokimyasal markerların diagnostic value araştırılması amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmada kronik hepatit B tanılı 248 hastaya ait karaciğer trucut biopsileri retrospektif olarak değerlendirilmiştir. Modifiye histolojik aktivite ve fibrozis skoru Ishak sınıflaması dikkate alınarak yapılmış olup hemogram ve biyokimyasal markerlarla karşılaştırılmıştır.

Bulgular: Fibrozis < 3 ve ≥3 gruplarını en iyi ayırt eden biyobelirteç %70.3 ayırt etme performansı ile aspartat aminotransferaz (AST) değeriydi. Histolojik aktivite indeksinde <6 ve ≥6 gruplarını en iyi ayırt eden biyobelirteçler, %75.5 ayırt etme performansı ile AST ve %73.7 ile alanine aminotransferaz (ALT) ve %73.4 ile gama-glutamil-transferaz değerleriydi.

Sonuç: Çalışmamızda kronik hepatit B vakalarında klinik pratikte kullanılan girişimsel olmayan markerların fibrozis ve nekroinflamatuar aktivitesini tahminde tanısal değere sahip olduğu gösterilmiştir.

Anahtar kelimeler: Kronik B hepatiti, histolojik aktivite indeksi, karaciğer fibrozisi, tam kan sayımı, biyokimya

-Yazışma Adresi/Address for Correspondence: Dr. Selma Erdoğan Düzcü, Bolu Abant Izzet Baysal University Medical School, Department of Pathology, Bolu, Turkey E-mail: serdoganduzcu@hotmail.com
Geliş tarihi/Received: 19.03.2021 Kabul tarihi/Accepted: 18.07.2021 Çevrimiçi yayın/Published online: 23.07.2021

INTRODUCTION

Chronic hepatitis B (CHB) infection is a chronic liver disease that accounts for millions of deaths each year[1]. Identification of the risk for liver fibrosis on CHB patients is necessary to determine antiviral therapy, prognosis, and potential risks[2,3]. Liver biopsy remains the gold standard for evaluation of fibrosis[1,4,5]. Patients with HBV-DNA $>10^5$ copies/ml and persistent or intermittent elevation in transaminase levels should be evaluated further with liver biopsy[6].

Although liver biopsy is a relatively safe procedure, it has a 0.2-2% morbidity rate (hemoperitoneum, pneumothorax, pain)[7]. However, due to the presence of limitations such as low platelet count, poor compliance, sampling error, and intra- and interobserver variability, there is a need for noninvasive, easy to perform, and inexpensive methods that can be used to predict liver histology[1,5,8]. Information about the diagnostic and prognostic value of hemogram and biochemical tests applied in routine practice in CHB is limited, and while studies emphasized fibrosis more, they did not consider the relation with necroinflammatory activity[9].

Since inflammation plays an important role in the progression of liver diseases, it is thought that inflammation-related parameters such as platelet-to-lymphocyte ratio (PLT/WBC), mean platelet volume (MPV), and mean corpuscular volume (MCV), might be used in predicting prognosis[9]. Platelet has a primary role in the progression of liver fibrosis, however, it has been shown that it has a negative correlation with fibrosis[8]. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values are frequently used to predict the stage of chronic hepatitis histologically, but their ideal cutoff values and accuracy are unclear[10]. Aspartate aminotransferase-to-platelet ratio index (APRI) has become a recently used model[2,4]. The World Health Organization (WHO) CHB guidelines recommend APRI to determine fibrosis stage in resource-limited countries[4].

In this study, we aimed to investigate the histological predictive value of hemogram and biochemical parameters in the evaluation of modified histological activity index (HAI) (developed by Ishak et al.) and fibrosis in liver biopsies[8]. In a limited number of studies in the literature, the relationship with fibrosis in CHB has been evaluated, and the evaluation of HAI in this study will contribute to the literature. It was hypothesized that these noninvasive parameters can be used to determine the degree of histological damage and fibrosis in the liver in CHB, and may guide the prognosis of the disease.

MATERIALS AND METHODS

Thi study has been approved by Bolu Abant Izzet Baysal University Ethic Committee for Clinical Research (2020/297).

Sample

In this study, liver tru-cut biopsies sent to Department of Pathology, Bolu Abant Izzet Baysal University, Faculty of Medicine between 2014-2020 were evaluated retrospectively. Of 410 liver biopsies in total, 248 cases diagnosed with CHB were included in the study. The cases with HCV, *human immunodeficiency virus* (HIV), hepatitis D virus (HDV), heart diseases, vascular diseases, chronic pulmonary diseases, renal diseases, diabetes mellitus, rheumatic diseases, hematologic diseases, malignant disease, drug use (antidiabetic, hyperlipidemic, antihypertensive, anticoagulant) were excluded from the study. According to these criteria, 45 patients were excluded from the study due to hepatitis C virus (HCV), 55 patients with malignant disease, 39 patients with autoimmune hepatitis and steatohepatitis, 18 patients with additional chronic diseases, and 5 patients due to drug use.

Of the CHB cases, the cases with the presence of hepatitis B surface antigen (HBsAg) in serum over six months and with serum HBV DNA >2000 IU/mL (measured by real-time PCR), and the cases for whom liver biopsy was performed for treatment planning purpose, were included in the study. The cases with HCV, *human immunodeficiency virus* (HIV), hepatitis D virus (HDV), heart diseases, vascular diseases, chronic pulmonary diseases, renal diseases, diabetes mellitus, rheumatic diseases, hematologic diseases, malignant disease, drug use (antidiabetic, hyperlipidemic, antihypertensive, anticoagulant) were excluded from the study.

Laboratory parameters

Patients' clinical information such as age and gender, hemogram and biochemical parameters, and HBV-related test results were obtained from archive records. Laboratory parameters included at most 2

week before biopsy. Hemogram parameters, were analyzed on Sysmex XN-1000 -hematology analyser (Kobe, Japan), such as MCV, mean corpuscular hemoglobin (MCH), mean platelet volume to platelet ratio (MPV/PLT), and PLT/WBC and biochemical parameters, were analyzed on Architect c8000 clinical chemistry analyser (Abbott, Illionis, USA), such as AST, ALT, gamma-glutamyl transferase (GGT), alcaline phosphatase (ALP), APRI were evaluated. The APRI score was calculated using the proposed formula; APRI=[(AST/ULN)/platelet] x 100[11].

Liver histology

The ultrasound-assisted percutaneous liver tru-cut biopsy specimens with a miminum length of 1.5 cm that composed of six portal areas were included in the study. These biopsy specimens were embedded into formalin-fixed paraffin blocks in a single center and stained with hematoxylin and eosin.

Necroinflammatory activity and fibrosis were scored using the scoring system developed by Ishak et al. According to this scoring system; HAI was calculated by evaluating the sum of four components (periportal or periseptal interface hepatitis [0-4], portal inflammation [0-4], focal lytic necrosis [0-4], and confluent necrosis [0-6]) over 18 [12]. Evaluation was made by dividing HAI score into two groups as <6 and ≥6.

Fibrosis was rated between 0-6. According to this scoring, the patients were seperated into two groups as F 0-2 (no fibrosis or mild fibrosis) and F 3-6 (moderate-severe fibrosis) [11]. In addition, fibrosis was evaluated using the Masson trichrome aniline blue (Facepath) and Reticulin-silver (Facepath) histochemical stain kits.

Statistical analysis

Mean and standard deviation or median and min-max values were used for descriptive statistics, while number and percentage values for categorical variables. The Kolmogorov-Smirnov test was used for normality assumption. The difference between the groups was examined by determining whether the difference between two mean scores was significant or using the Mann-Whitney U test. The Pearson's or Spearman's correlation coefficient was used to determine whether there was a significant relationship between numerical variables. The area under the ROC curve (AUC) was used to evaluate the performance of bioparameters to distinguish groups. The level of significance was accepted as $p<0.05$. Analyzes were performed using IBM SPSS Statistics for Windows, version 21.0 (Armonk, NY: IBM Corp.)

RESULTS

Of 248 patients examined in the study; 104 (41,9%) were female. The mean age was 46.6 ± 12.77 (20-80) years. HbeAg was negative in 157 (84.4%) patients and positive in 29 (15.6%) patients. The patients' mean HBV-DNA was 118.055.994± SD IU/ml. The liver biopsies were composed of 12 ± SD portal areas and the mean length of liver biopsy was 2,88± SD cm. The mean HAI score was 5,8± SD and there were 163 (65.7%) patients with < 6 HAI score and 85 (34.3%) patients with ≥6 HAI score while the mean fibrosis score was 2,0± SD and there where 128 (51.6%) patients with < 3 and 120 (48.4%) with ≥3 values. Figure 1a-d shows the images of low/high HAI and fibrosis groups.

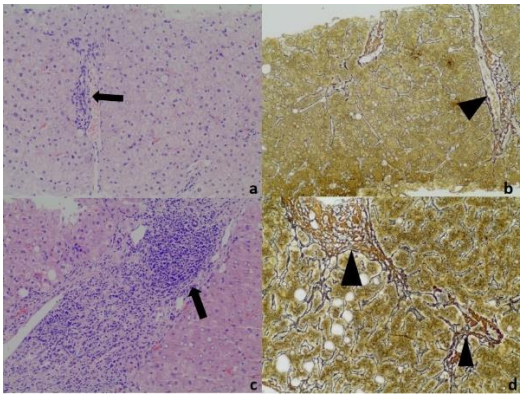

Figure 1: a: Mild portal inflammation in low HAI and fibrosis group, HEX200 b: Mild fibrosis in low HAI and fibrosis group, ReticulinX200 c: Acute portal inflammation in high HAI and fibrosis group, HEX200 d: Significant fibrosis in high HAI and fibrosis group, ReticulinX200.

A significant relationship was found between portal inflammation, periportal interface hepatitis, focal lytic necrosis, and HAI with AST (r=0.463, r=0.436, r=0.368 and r=0.488, respectively), ALT (r=0.384, r=0.379, r=0.302 and r=0.424, respectively), GGT (r=0.494, r=0.405, r=0.304 and r=0.449, respectively), APRI values (r=0.376, r=0.356, r=0.233 and r=0.376, respectively). There was very low relationship between confluent necrosis and other parameters. Table 1 shows the relationship of

HAI, fibrosis values with hemogram and biochemical parameters.

In fibrosis groups, significant differences were found in terms of the levels of MCV, MCH, AST, ALT, GGT, ALP and APRI, and these were lower in the group with fibrosis values <3. Table 2 shows the relationship between fibrosis groups and parameters.

Among the HAI groups, there was a significant difference in terms of the values of MCV, MCH, MPV / PLT, AST, ALT, GGT, and APRI. These values of the group with HAI values <6 were lower. In the HAI groups, there was a significant difference in PLT/WBC, AST/ALT values. The values were higher in the group with HAI group <6. Table 3 shows the relationship between HAI groups and parameters.

In the fibrosis groups, the AST value was the best marker to discriminate < 3 ve ≥3 groups, with 70.3% discrimination performance ($p<0.001$). In the HAI groups, AST, ALT, and GGT was most significant parameters to discriminate <6 ve ≥6 groups with 75.5%, 73.7%, and 73.4% discrimination performances, respectively ($p<0.001$). Table 4 shows the ROC analysis of the performance of parameters to discriminate fibrosis and HAI groups.

Tablo 1. Relationship between diagnostic parameters HAI and fibrosis

	Portal inflamation	Periportal interface hepatitis	Focal lytic necrosis	Confluent necrosis	HAI	Fibrosis
PLT (K/uL)	-0.162*	-0.153*	-0.016	-0.088	-0.123	-0.101
MCV (fL)	0.084	0.159*	0.095	0.129	0.147	0.121
MCH (pg)	0.115	0.225**	0.080	0.179*	0.193**	0.112
MPV (fL)	0.093	0.153*	-0.030	0.133	0.121	0.024
PLT / WBC	-0.152*	-0.218**	-0.045	-0.167*	-0.181**	-0.091
MPV / PLT (x100)	0.209**	0.249**	0.064	0.114	0.200**	0.157
AST (U/L)	0.463**	0.436**	0.368**	0.180**	0.488**	0.358**
ALT (U/L)	0.384**	0.379**	0.302**	0.174**	0.424**	0.301**
GGT (U/L)	0.494**	0.405**	0.304**	0.221**	0.449**	0.334**
ALP (U/L)	0.213**	0.118	0.055	0.089	0.120	0.302**
APRI	0.376**	0.356**	0.233**	0.167**	0.376**	0.296**

* <0.05 ** <0.01

(PLT: platelet, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MPV: mean platelet volume, WBC: white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, ALP: alcaline phosphatase, APRI: Aspartate aminotransferase-to-platelet ratio index)

Tablo 2. Comparison of parameters with liver biopsy fibrosis scores

	Fibrosis		p
	< 3 (n=128)	≥3 (n=120)	
PLT (K/uL)	217 [81.6 - 421]	208 [80.4 - 1263]	0.409
MCV (fL)	88.7 [72.5 - 102]	89.15 [60.3 - 102]	0.048
MCH (pg)	29.2 [22.8 – 34.8]	30.0 [19.3 – 34.2]	0.049
PLT / WBC	32.31 [6.28 – 64.91]	31.02 [9.59 – 82.10]	0.444
MPV / PLT (x100)	3.65 [0.0 – 10.43]	3.84 [0.61 – 11.55]	0.159
AST (U/L)	23.0 [8.0 - 1055]	34.0 [13.0 - 1694]	<0.001
ALT (U/L)	26.0 [11.0 - 2109]	39.0 [12.0 - 3039]	<0.001
GGT (U/L)	18.0 [7.0 – 325.0]	26.0 [8.0 – 663.0]	0.005
ALP (U/L)	69.0 [32.0 – 262.0]	77.0 [40.0 – 834.0]	0.014
APRI	0.296 [0.0 – 14.234]	0.442 [0.0 – 25.163]	<0.001

(PLT: platelet, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MPV: mean platelet volume, WBC: white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, ALP: alcaline phosphatase, APRI: Aspartate aminotransferase-to-platelet ratio index)

Tablo 3. Comparison of parameters with liver biopsy HAI scores

	HAI		p
	< 6 (n=163)	**≥6 (n=85)**	
PLT (K/uL)	217.5 [83.0 - 421]	206 [80.4 - 1263]	0.066
MCV (fL)	88.55 [68.4 – 98.1]	89.6 [60.3 - 102]	**0.016**
MCH (pg)	29.2 [22.3 – 34.8]	29.9 [19.3 – 34.2]	**0.022**
PLT / WBC	33.44 [14.87 – 82.09]	30.593 [6.277 – 72.10]	**0.007**
MPV / PLT (x100)	3.55 [0.0 – 10.43]	4.018 [0.0 – 11.55]	**0.011**
AST (U/L)	22.0 [8.0 - 140]	34.0 [14.0 - 1694]	**<0.001**
ALT (U/L)	23.0 [11.0 - 223]	45.0 [11.0 - 3039]	**<0.001**
GGT (U/L)	17.0 [7.0 – 402.0]	28.0 [7.0 – 663.0]	**<0.001**
ALP (U/L)	70.0 [32.0 – 262.0]	72.0 [38.0 – 834.0]	0.604
AST / ALT	0.928 [0.271 – 2.154]	0.763 [0.152 – 3.13]	**<0.001**
APRI	0.290 [0.0 – 1.72]	0.479 [0.0 – 25.16]	**<0.001**

(PLT: platelet, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MPV: mean platelet volume, WBC: white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, ALP: alcaline phosphatase, APRI: Aspartate aminotransferase-to-platelet ratio index)

Tablo 4.ROC analysis of the performance of the parameters to discriminate fibrosis and HAI groups

	AUC	**%95 GA**	**p**
Fibrosis			
MCV	0.577	0.499 – 0.654	0.052
MCH	0.577	0.495 – 0.658	0.066
AST	0.703	0.632 – 0.773	<0.001
ALT	0.656	0.581 – 0.731	<0.001
GGT	0.633	0.543 – 0.723	0.004
ALP	0.619	0.526 – 0.711	0.012
APRI	0.662	0.589 – 0.735	<0.001
HAI			
MCV	0.588	0.524 – 0.650	0.015
MCH	0.584	0.520 – 0.646	0.021
PLT /WBC	0.599	0.535 – 0.661	0.006
MPV / PLT	0.593	0.529 – 0.655	0.010
AST	0.755	0.694 – 0.809	<0.001
ALT	0.737	0.674 – 0.793	<0.001
GGT	0.734	0.661 – 0.799	<0.001
AST / ALT	0.637	0.570 – 0.699	<0.001
APRI	0.697	0.636 – 0.754	<0.001

(PLT: platelet, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MPV: mean platelet volume, WBC: white blood cell, ALT: alanine aminotransferase, AST: aspartate aminotransferase, GGT: gamma-glutamyl transferase, ALP: alcaline phosphatase, APRI: Aspartate aminotransferase-to-platelet ratio index)

DISCUSSION

Chronic hepatitis B is still one of the leading causes of cirrhosis and hepatocellular carcinoma worldwide and the gold-standard method to assess the severity of liver fibrosis[13]. According to HAI developed by Ishak, which has a prognostic importance in the histological evaluation of chronic hepatitis, grading that determines necroinflammatory activity and staging that determines fibrosis is made semi-quantitatively[12].

Liver biopsy has a lot of advantages for obtaining direct information not only about fibrosis, but also about many useful parameters, such as inflammation, necrosis, and steatosis [1]. In recent years, noninvasive parameters have been examined for estimating the severity of liver fibrosis in patients with chronic hepatitis B[8]. However, it was stated that it cannot be

applied directly to CHB patients due to the different histology and clinical course of parameters applied in hepatitis C and that these parameters should be validated[7,11,14]. Due to the lack of the studies examining CHB patients and failure to use of some of non-invasive methods in routine practice, satisfying results were not obtained in detecting fibrosis[5,15].

Although the role of platelets in progression of fibrosis is not clear, however, it has been shown that in a negative correlation with platelets, decrease in profibrogenic transforming growth factor-beta expression and increase in matrix metalloproteinase expression may alleviate liver fibrosis [8]. Since interleukin-6 (IL-6), secreted in inflammation in CHB, can increase megakaryopoiesis, it increases MPV levels and platelet production as a result of increased young platelets[1,16].

In their study examined 111 patients, Ceylan et al. revealed that MPV is an independent variable in determining the severity of inflammation rather than liver fibrosis[16]. They observed that MPV was lower among patients with severe fibrosis and stated that lower MPV might be due to severe inflammation in patients with severe fibrosis[16]. Hakyemez et al. suggested that MPV and MPV/PLT have an important role in predicting fibrosis in CHB patients[8]. Ekiz et al. showed that MPV increased while platelets decreased in more severe fibrosis stage in patients with CHB [1]. Karagöz et al. found that MPV is associated with advanced fibrosis[13]. While MPV shows an increase in inflammation, its increase has been associated with mortality and poor prognosis in the limited studies examining the relationship of MCV with liver disease[9]. PLT/WBC is used to predict inflammation and mortality[9]. In our study, on the other hand, we found that MCV and MCH values were higher in high HAI and fibrosis groups and that these parameters were associated with both the fibrosis stage and necroinflammatory activity. While there was no relationship between PLT/WBC, MPV/PLT ratios and fibrosis, the higher rates in higher HAI scores suggests that these parameters may be indicative of inflammatory processes.

There are studies on HAI, fibrosis score and serum aminotransferases with different results[17]. When the liver is damaged, AST and ALT is released into the bloodstream and its increased level is an indicator of hepatic damage[18]. ALT is a liver-specific enzyme that is found only in liver and shows high sensitivity in inflammation, necrosis, vacuolar degeneration and neoplasia[17]. Ozkara et al. found that AST and ALT levels in patients with CHB are associated with HAI and fibrosis[17].

GGT is a microsomal enzyme that can be isolated from hepatocytes and gall bladder epithelium, and increases in GGT values occur in various liver, gall bladder, and pancreatic diseases[10]. Eminler et al. found that GGT showed a significant increase with HAI and the degree of fibrosis [10]. However, they did not find a significant difference between ALT, AST, and ALP levels in HAI groups[10]. They proposed that GGT levels can be taken into consideration to predict advanced histological liver damage[10]. In their study on patients with chronic hepatitis, Guclu et al. identified AST and ALP as independent risk factors and they proposed that AST is more useful than ALT in demonstrating liver damage[18].

In our study, we found the levels of AST, ALT, and GGT as high in the high HAI and fibrosis group. The high level of ALP showed a significant difference in the high fibrosis group but not a significant difference in the high HAI group. These results supported that AST, ALT and GGT were predictive for both fibrosis and necrorinflammatory activity, while ALP could be an indicator of inflammation.

In their study conducted with 120 HBV patients, Ormeci et al. considered the patients with HBV DNA levels between 2000 and 20 000 IU/ml and normal ALT as within the 'gray zone'[19]. They recommended that noninvasive methods such as APRI, fibrosis 4 score, and vibration-controlled transient elastograhpy might be used in these 'gray zone' patients[19]. Wai et al., who first evaluated the APRI score in CHB cases, underlined that although the platelet count tends to decrease as fibrosis increases, APRI may be insufficient to fully indicate fibrosis in CHB as overlaps might also be seen with increased fibrosis levels[7]. In our study, similar to the study of Wai et al., we could not find a relationship with platelet count, but we found that AST and APRI scores increased significantly in high HAI and fibrosis stages.

Peng et al. noted that the APRI score increased in hepatic fibrosis[2]. They found that APRI score decreased in patients treated with nucleoside analogue compared to interferon-treated patients[2]. Gumusay et al. stated that APRI is a simple and noninvasive test to evaluate liver fibrosis[3]. Although Celikbilek et al. found the APRI score higher in

patients with significant fibrosis, they could not identify a statistically significant difference[20].

In their metaanalysis study, Jin et al. highlighted that the AUC of APRI were more likely fluctuated from 0.75 to 0.9 and thus, it is not a good indicator that can be used to show significant fibrosis and cirrhosis, and that it would not decrease the number of liver biopsy[21]. Kim et al. suggested that APRI is associated with increasing fibrosis stage, but cannot replace liver biopsy due to the complex histological structure of HBV[4]. Güzelbulut et al. revealed that APRI was higher and platelet count was low in patients with significant fibrosis[11]. Sebastiani et al. found that when APRI and Fibrotest were combined with liver biopsy in sequential algorithms, they could reach > 95% accuracy for detecting significant fibrosis or cirrhosis[6]. Kim et al. indicated that AST/ALT and APRI were associated with the fibrosis stage[14].

In our study, in accordance with the literature, in addition to finding also the APRI score high in the high fibrosis group, we also determined a significant increase in the APRI score in the high HAI groups which was not pointed out in the literature. However, the AUROC for HAI and fibrosis was 0.662 and 0.697, and we found that they were lower than the literature data.

In our study, based on the ROC analysis results, the best predictive parameters for fibrosis were AST, and the best predictive parameters for HAI were AST, ALT and GGT, respectively, and we believe that these parameters can be noninvasive parameters that can be used to predict liver necroinflammatory activity and fibrosis stage in CHB.

This study has some limitations. This was a retrospective and single-centered study so there were limited sample size.

In our study, we suggested that noninvasive parameters used in clinical practice are related to varying degrees with liver necroinflammatory activity and increased fibrosis. We believe that the use of these parameters alone or in combination as predictive factors has an important role in determining histological liver damage progression. The outcome of this study necessitated more comprehensive prospective studies in noninvasive parameters in CHB cases.

Yazar Katkıları: Çalışma konsepti/Tasarımı: SED, ŞÖ; Veri toplama: SED, ŞÖ; Veri analizi ve yorumlama: SED, ŞÖ; Yazı taslağı: SED, ŞÖ; İçeriğin eleştirel incelenmesi: SED, ŞÖ; Son onay ve sorumluluk: SED, ŞÖ; Teknik ve malzeme desteği: SED; Süpervizyon: SED; Fon sağlama (mevcut ise): yok.

Etik Onay: Bu çalışma için Bolu Abant İzzet Başsal Üniversitesi Klinik Araştırmalar Etik Kurulundan 08.12.2020 tarih ve 2020/297 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : SED, ŞÖ; Data acquisition: SED, ŞÖ; Data analysis and interpretation: SED, ŞÖ; Drafting manuscript: SED, ŞÖ; Critical revision of manuscript: SED, ŞÖ; Final approval and accountability: SED, ŞÖ; Technical or material support: SED; Supervision: SED; Securing funding (if available): n/a.
Ethical Approval: Ethical approval was obtained for this study from the Clinical Research Ethics Committee of Bolu Abant İzzet Başsal University with the decision dated 08.12.2020 and numbered 2020/297.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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