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HCV ENFEKSİYONLU NAİF HASTALARDA TAM KAN SAYIMI PARAMETRELERİ İLE KARACİĞER HİSTOLOJİSİ ARASINDAKİ İLİŞKİNİN DEĞERLENDİRİLMESİ

ASSESSMENT OF RELATIONSHIP BETWEEN COMPLETE BLOOD COUNT PARAMETERS AND LIVER HISTOLOGY IN TREATMENT NAIVE PATIENTS WITH HCV INFECTION

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Anahtar Sözcükler: Hepatit C virüsü (HCV), karaciğer histolojisi, fibrozis, tam kan sayımı parametreleri
Keywords: Hepatitis C virus, liver histology, fibrosis, complete blood count parameters

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ÖZ

Giriş: *Hepatit C virüsü (HCV) enfeksiyonlu tedavi görmemiş naif erkek hastalarda, platelet-lenfosit (PLR), nötrofil-lenfosit (NLR) ve RDW-platelet (RPR) oranı gibi tam kan sayımı (CBC) parametreleri ve oranları ile karaciğer histolojisi arasındaki ilişkiyi araştırmayı amaçladık.*

Gereç ve Yöntem: *Biyopsi ile kanıtlanmış daha önce tedavi görmemiş naif kronik HCV enfeksiyonu olan erkek hastalar çalışmaya alındı. Değişkenlerdeki farklılığı değerlendirmek için hastalar fibrozis skorlarına göre fibrozisi olmayan veya minimal fibrozis grubu (fibrozis skoru <2) ve ileri fibrozis grubu (fibrozis skoru≥2) olmak üzere 2 gruba ayrıldı. Ayrıca hastalar histolojik aktivite indeksi (HAI) skoruna göre HAI <7 grubu ve HAI> 6 grubu olarak 2 gruba ayrıldı. Anlamlı fibrozu tahmin etmek için, kırmızı hücre dağılım genişliği (RDW), ortalama trombosit hacmi (MPV) ve plateletkrit (PCT) dahil olmak üzere hastaların tam kan parametrelerinin kullanılabilirliğini araştırdık.*

Bulgular: *Çalışmaya ortalama yaşları 23.95 ± 5.42 yıl olan 78 erkek tedavi almamış naif HCV hastası alındı. İleri fibrozlu hastalarda, fibrozsizi olmayan veya minimal fibrozlu gruba göre MPV ve PCT değerleri (sırasıyla; p = 0,006 ve p = 0,046) anlamlı olarak daha düşükken, PLR, NLR ve RPR gibi diğer tam kan parametre ve oranları açısından iki grup arasında fark saptanmamıştır. Ayrıca HAI skorlarına göre gruplar arasında tüm değişkenlerde fark yoktu.*

Sonuç: *MPV ve PCT'nin tedavi almamış naif HCV hastalarında fibrozun şiddetini tanımlayan skorlama sistemlerinde kullanılabileceğini düşünüyoruz, ancak randomize geniş ölçekli çalışmalara ihtiyaç vardır.*

SUMMARY

Introduction: *We aimed to investigate the relationship between liver histology and complete blood count parameters (CBC) parameters or ratios such as platelet-to-lymphocyte (PLR), neutrophil-to-lymphocyte (NLR) and RDW-to-platelet ratio (RPR) in treatment naive male patients with hepatitis C virus (HCV) infection.*

Material and Method*: Treatment naive biopsy-proven male patients with chronic HCV infection were enrolled in the study. For evaluating the difference in variables, patients were divided into 2 groups such as no or minimal fibrosis group (fibrosis score<2) and significiant fibrosis group (fibrosis score≥2) according to their fibrosis scores, and also patients were divided into 2 groups according to their histological activity index (HAI) scores such as*

HAI<7 group and HAI>6 group. To predict significiant fibrosis, we also investigated the usability patients' CBC parameters including complete red cell distribution width (RDW), mean platelet volume (MPV) and plateletcrit (PCT).

***Results:** 78 male treatment naive HCV patients with a mean age of 23.95±5.42 years were enrolled in the study. MPV and PCT values were significiantly (respectively; p=0.006, and p=0.046) lower in patients with significiant fibrosis compared with no or minimal fibrosis group, while there was no difference in the other complete blood count parameters or ratios such as PLR, NLR and RPR between two groups. Moreover, there was no difference in all variables between groups according to HAI scores.*

***Conclusion**: We think that MPV and PCT can be used in scoring systems defining severity of fibrosis in treatment naive HCV patients, but randomized large-scale studies are required.*

INTRODUCTION

Hepatitis C is a liver infection caused by the hepatitis C virus (HCV). It is is an important public health problem. World Health Organization (WHO) estimates that approximately 100 million people are infected with HCV globally, of which 71 million have chronic HCV hepatitis. In addition, HCV virus causes hepatocellular carcinoma (HCC) and cirrhosis (1). Although there are other non-invasive tests for grading and staging of liver histology, percutaneous liver biopsy is still the gold standard method. However, since it is an invasive procedure, it is open to complications. In addition, errors in sampling, lack of standardization in staging, and staging according to pathologist are other disadvantages. The necessity of repeating the biopsy in order to evaluate the response to treatment after treatment and to determine the prognosis, and the necessity of hospitalization cause an increase in cost. (2). Thus, there are several studies to find non-invasive methods that can be used instead of percutaneous liver biopsy (2, 3).

Complete blood count (CBC) can easily be performed and contain white blood cell parameters such as neutrophile count and lymphocyte count, or red blood cell (RBC) count and indices including red cell distribution width (RDW), or platelet count and indices such as mean platelet volume (MPV), platelet volume distribution width (PDW), and plateletcrit (PCT).

RDW, a measure of the range of variation in circulating RBC volume, has been shown to be increased or to be related to fibrosis in patients with nonalcoholic steatohepatitis, primary biliary cirrhosis or primary viral hepatitis (4-9).

Platelets, which primarily function in hemostasis, also have an important function in the inflammatory response. Although the size and number of platelets may vary in the presence of infection, they may vary in parallel with the severity of the infection. This is also observed in primary viral hepatitis, regardless of the etiologic agent. CBC parameters related to thrombocyte; MPV shows the mean volume of platelets and platelet activation, while PDW shows the distribution in platelet size. PCT is a reliable parameter of platelet biomass and is affected by platelet count and size. There are several studies investigating whether these platelet indices are predictors or useful markers of liver histology with questionable findings (4, 8-17).

There are also ratios, calculated from CBC parameters, such as platelet-to-lymphocyte (PLR), neutrophil-to-lymphocyte (NLR) and RDW-to-platelet ratio (RPR). NLR and PLR have been evaluated in a wide variety of disease groups. There are studies evaluating these parameters in many diseases from infectious diseases including viral hepatitis, cardiovascular diseases, malignancies, chronic inflammatory diseases, malignancies. (5, 10, 16-20). Furthermore, NLR has been reported to be negatively correlated with histological activity index (HAI) score or to be correlated with HCV ribonucleic acid (RNA) levels (5, 20). Also, RPR values have been shown to be significiantly higher in patients with primary biliary cirrhosis, HCV or HBV, associated with severity (4, 8, 9, 21, 22).

In the light of these literature findings, we aimed to research the relationship between liver histology and CBC parameters or ratios calculated from CBC parameters in treatment naive male patients with HCV infection.

MATERIAL AND METHOD

Patients and data

Before starting the study, an application was made to the Gulhane Medical Faculty General Ethics Committee and Publication Ethics Committee, which are the committee (institutional and national) responsible for human experiments. As a result of the evaluation made by the committee, it was found in accordance with the Declaration of Helsinki and an ethical approval letter was given (2016/304).

Chronic HCV patients were evaluated retrospectively. Treatment naive biopsy-proven male patients with chronic HCV infection were enrolled in the study. Inadequate liver sample and inaccessible laboratory results as well as the presence of human immunodeficiency virus (HIV) or HBV coinfection were determined as exclusion criteria. In addition, patients with certain comorbidities (other infectious diseases, malignancy, myeloproliferative diseases, metabolic disorders, chronic inflammatory diseases, corticosteroid use, alcohol abuse, hepatosteatosis, etc.) were excluded from the study.

The data including patients' age, serum AST, ALT and HCV RNA levels, fibrosis and HAI scores, and CBC parameters including neutrophile counts, lymphocyte counts, platelet counts, RBC counts, values of RDW, MPV, PDW and PCT were recorded. Laboratory data obtained from blood samples studied in preparation for liver biopsy were used. Also, PLR, NLR and RPR were calculated using the values of neutrophile count, lymphocyte count, platelet count and RDW values obtained from patients' CBC results.

In the light of our findings and the literature, to predict significiant fibrosis, we also investigated new scoring systems calculated using patients' serum AST levels, age, RDW, MPV and PCT levels on the following formulas:

AST-to-MPV ratio (AMR): AST (U/l) / MPV (fl)

AST-to-PCT ratio (APTR): AST (U/l) / PCT (%)

AMRage: [AST (U/l)×Age (years)] / MPV (fl)

APTRage: [AST (U/l)×Age (years)] / PCT (%)

RDW-to-MPV ratio (RMR): RDW (%) / MPV (fl)

RDW-to-PCT ratio (RPTR): RDW (%) / PCT (%)

RMRage: [RDW (%)×Age (years)] / MPV (fl)

RPTRage: [RDW (%)×Age (years)] / PCT (%)

AST-RMR: [AST (U/l)×RDW (%)] / MPV (fl)

AST-RPTR: [AST (U/l)×RDW (%)] / PCT (%)

AST-RMRage: [AST (U/l)×RDW (%)×Age (years)] / MPV (fl)

AST-RPTRage: [AST (U/l)×RDW (%)×Age (years)] / PCT (%)

The Ishac scoring system was used to calculate the HAI score and the fibrosis score. We defined significiant fibrosis as fibrosis score≥2. Then the patients were divided into 2 groups according to their HAI score and fibrosis score. Evaluations between variables were made on these groups. According to the fibrosis score, they were divided into two groups as no fibrosis or minimal fibrosis group (fibrosis score<2) and significant fibrosis group (fibrosis score≥2), while groups were determined as HAI<7 group and HAI>6 group according to HAI score.

Statistical analyses

SSPS 23.0 (SSPS Inc., Chicago, ILL., USA) program was used for statistical analysis. Using the GPower 3.1 program, when the power of the study was 0.80, the error level was 0.05, and the effect size was 0.32, when the sample size was calculated, 79 patients were required to be reached. Whether the data conformed to the normal distribution was determined according to analytical and visual methods. While Kolmogorov-Smirnov and Shapiro-Wilk tests were used as analytical methods, on the other hand histograms and probability plots were used. The method to be used for the assessment of continuous variables, comparison and correlation between variables was determined depending on the normalcy of the data distribution. Continuous variables were summarized with mean±standard deviation or median [interquartile range (Iq)] values, while comparisons with Mann-Whitney U test or Student's t test were made. Correlations between variables were also analyzed with the Pearson test or the Spearman correlation test. In the analysis data obtained, $p<0.05$ value was considered statistically significant.

The validity of the scores in predicting high fibrosis was evaluated. For this, ROC (Receiver Operating Characteristics) curve analysis was used.

RESULTS

Overall, 78 male treatment-naive patients with chronic HCV infection were enrolled in the study. The mean age of the patients included in the study was 23.95±5.42 years, the median age (interquartile range) was 21 (3) years, and the age range was 20-41 years. The main characteristics of the patients are listed in Table 1.

There wasn't correlation between PLR and HCV RNA (r=-0.013, p=0.911), NLR and HCV RNA (r=0.096, p=0.401), RPR and HCV RNA (r=-0.168 p=0.141), MPV and HCV RNA (r=0.066, p=0.568), PCT and HCV RNA (r=0.159 p=0.166), RDW and HCV RNA (r=-0.160, p=0.161), PDW and HCV RNA (r=-0.121, p=0.290), PLR and HAI score (r=-0.076, p=0.509), NLR and HAI score (r=-0.005, p=0.965), RPR nd HAI score (r=-0.073, p=0.527), MPV and HAI score (r=-0.021, p=0.857), PCT and HAI score (r=0.033 p=0.777), RDW and HAI score (r=0.065, p=0.572), or PDW and HAI score (r=-0.020, p=0.862).

Thirteen patients (16.7%) included in the study had a fibrosis score of 0, 30 patients (38.5%) had a fibrosis score of 1, 28 patients (35.9%) had a fibrosis score of 2, and 7 patients (9%) had a fibrosis score of 3. According to fibrosis scores, patients were divided into 2 groups such as no or minimal fibrosis group (fibrosis score<2) and significiant fibrosis group (fibrosis score≥2). While 43 (55.1%) of the patients were in the group with no or minimal fibrosis, 35 patients (44.9%) were in the group with significant fibrosis. According to HAI scores, there were 54 patients (69.2%) in HAI<7 group and 24 patients (30.8%) in HAI>6 group. Results of complete blood count parameters and ratios in groups according to fibrosis scores and in groups according to HAI scores were described respectively in Table 2 and in Table 3. There were only difference in MPV and PCT values between groups according to fibrosis score. MPV and PCT values were significiantly lower in patients with significiant fibrosis compared with no or minimal fibrosis group (respectively; p=0.006, and p=0.046) (Table 2). However, there was no difference in all variables between HAI<7 group and HAI>6 group (Table 3).

In the light of these results and literature, for predicting significiant fibrosis, we also investigated new scoring systems calculated using patients' serum AST levels, age, RDW, MPV and PCT levels. As a result of ROC curve analysis, we determined that as a predictor of significiant fibrosis (fibrosis score≥2) in treatment-naive HCV patients, area under ROC curve (AUROC) for AMR was 0.735 (p<0.001), AUROC for APTR was 0.765 (p<0.001), AUROC for AMRage was 0.769 (p<0.001), AUROC for APTRage was 0.799 (p<0.001), AUROC for RMR was 0.655 (p=0.019), AUROC for RPTR was 0.644 (p=0.030), AUROC for RMRage was 0.707 (p=0.002), AUROC for RPTRage was 0.703 (p=0.002), AUROC for AST-RMR was 0.724 (p=0.001), AUROC for AST-RPTR was 0.760 (p<0.001), AUROC for AST-RMRage was 0.755 (p<0.001), and lastly AUROC for AST-RPTRage was 0.793 (p<0.001) ((Figure 1 and Figure 2).

The area under the ROC curve determines the accuracy of the test in distinguishing between patients and non-patients. The size of the area under the ROC curve indicates the statistical significance of the discrimination ability of the diagnostic test studied. The expected value of the area under the ROC curve is 0.50 when the diagnostic test being studied has no discrimination ability. In the interpretation of the areas under the curve, 0.50-0.60 can be interpreted as unsuccessful, 0.60-.70 weak, 0.70-0.80 moderate, 0.80-0.90 good, 0.90-1.00 excellent.

In our study findings, it was concluded that since the highest ROC curve area of 0.79 corresponds to the middle level, a new scoring system cannot be created directly with the above-mentioned parameters.

Table 1. Baseline characteristics of patients (n=78).

Variables	Mean±standard deviation	(Min.-Max.)	Median (interquartile range)
Age (Years)	23.95±5.42	(20-41)	21 (3)
RBC (10^6/mm^3)	5.16±0.37	(4.37-6.13)	5.12 (0.52)
Neutrophile (10^3/mm^3)	4.14±1.26	(2.10-8.49)	4.00 (1.47)
Lymphocyte (10^3/mm^3)	2.45±0.84	(0.70-7.10)	2.29 (0.94)
Platelet (10^3/mm^3)	261.08±59.21	(150-428)	249 (75)
RDW (%)	13.90±1.92	(11.50-21.70)	13.45 (1.50)
MPV (fl)	9.87±9.02	(5.70-87)	8.70 (1.30)
PCT (%)	0.227±0.051	(0.135-0.384)	0.220 (0.056)
PDW (%)	18.32±10.15	(9.50-55.50)	15.05 (3.38)
NLR	1.81±0.70	(0.80-4.36)	1.60 (0.70)
PLR	116.04±42.98	(49.86-296.40)	104.66 (43.64)
RPR	0.055±0.011	(0.03-0.09)	0.053 (0.010)
AST (U/l)	54.92±30.17	(14-173)	45.50 (47)
ALT (U/l)	91.97±67.24	(7-308)	71 (100)
HCV RNA (log_{10} IU/ml)	5.75±1.08	(14-173)	5.90 (1.57)
Fibrosis Score	1.37±0.87	(0-3)	1 (1)
HAI score	5.55±1.82	(1-10)	6 (3)

RBC: Red blood cell count, RDW: Red cell distribution width, MPV: Mean platelet volüme, PCT: Plateletcrit, PDW: Platelet volume distribution width, NLR: Neutrophile-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, RPR: Red cell distribution width-to-platelet ratio, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, HCV RNA: Hepatitis C virus ribonucleic acid levels, HAI: Histological activity index

Table 2. Results of complete blood count parameters in groups according to fibrosis scores.

Variables	No or Minimal fibrosis (Fibrosis score < 2) n=43 (55.1%)	Significiant fibrosis (Fibrosis score ≥ 2) n=35 (44.9%)	p Value
Age (Years)	21	22	0.082
RBC (10^6/mm^3)	5.13±0.38	5.20±0.35	0.430
Neutrophile (10^3/mm^3)	3.96±1.04	4.35±1.47	0.171
Lymphocyte (10^3/mm^3)	2.28	2.30	0.721
Platelet (10^3/mm^3)	263.26±63.87	258.40±53.72	0.721
RDW (%)	13.40	13.60	0.813
MPV (fl)	9	8.30	0.006
PCT (%)	0.237	0.210	0.046
PDW (%)	15.10	14.90	0.740
NLR	1.58	1.73	0.190
PLR	104.70	104.62	0.775
RPR	0.055±0.011	0.055±0.011	0.871

RBC: Red blood cell count, RDW: Red cell distribution width,MPV: Mean platelet volüme,PCT: Plateletcrit,PDW: Platelet volume distribution width,NLR: Neutrophile-to-lymphocyte ratio,PLR: Platelet-to-lymphocyte ratio,RPR: Red cell distribution width-to-platelet ratio

Table 3. Results of complete blood count parameters in groups according to HAI scores.

Variables	HAI score < 7 n=54 (69.2%)	HAI score > 6 n=24 (30.8%)	p Value
	Mean±Standart Deviation (Minimum-Maximum) or Median (interquartile range) (Minimum-Maximum) *		
Age (Years)	21 (2) (20-39)	21.50 (10) (20-41)	0.247
RBC (10^6/mm^3)	5.14±0.39 (4.37-6.13)	5.20±0.32 (4.62-6.07)	0.535
Neutrophile (10^3/mm^3)	4.04±1.25 (2.10-8.49)	4.36±1.27 (2.42-7.10)	0.303
Lymphocyte (10^3/mm^3)	2.24 (1.07) (0.70-3.80)	2.32 (0.81) (1.46-7.10)	0.918
Platelet (10^3/mm^3)	259.19±60.26 (150-417)	265.33±57.80 (189-428)	0.675
RDW (%)	13.35 (1.23) (11.50-21.70)	13.85 (2.08) (11.70-21.30)	0.279
MPV (fl)	8.80 (1.78) (5.70-87)	8.60 (1.18) (6.70-10.20)	0.274
PCT (%)	0.222 (0.063) (0.135-0.360)	0.215 (0.063) (0.148-0.384)	0.705
PDW (%)	14.95 (3.38) (9.50-55.50)	15.40 (3.78) (9.50-46)	0.862
NLR	1.59 (0.67) (0.85-4.01)	1.61 (0.80) (0.80-4.36)	0.833
PLR	104.46 (46.70) (52.53-296.40)	106.92 (41.20) (49.86-170.55)	0.871
RPR	0.055±0.012 (0.03-0.09)	0.055±0.009 (0.03-0.07)	0.913

RBC: Red blood cell count, RDW: Red cell distribution width, MPV: Mean platelet volüme, PCT: Plateletcrit, PDW: Platelet volume distribution width, NLR: Neutrophile-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, RPR: Red cell distribution width-to-platelet ratio

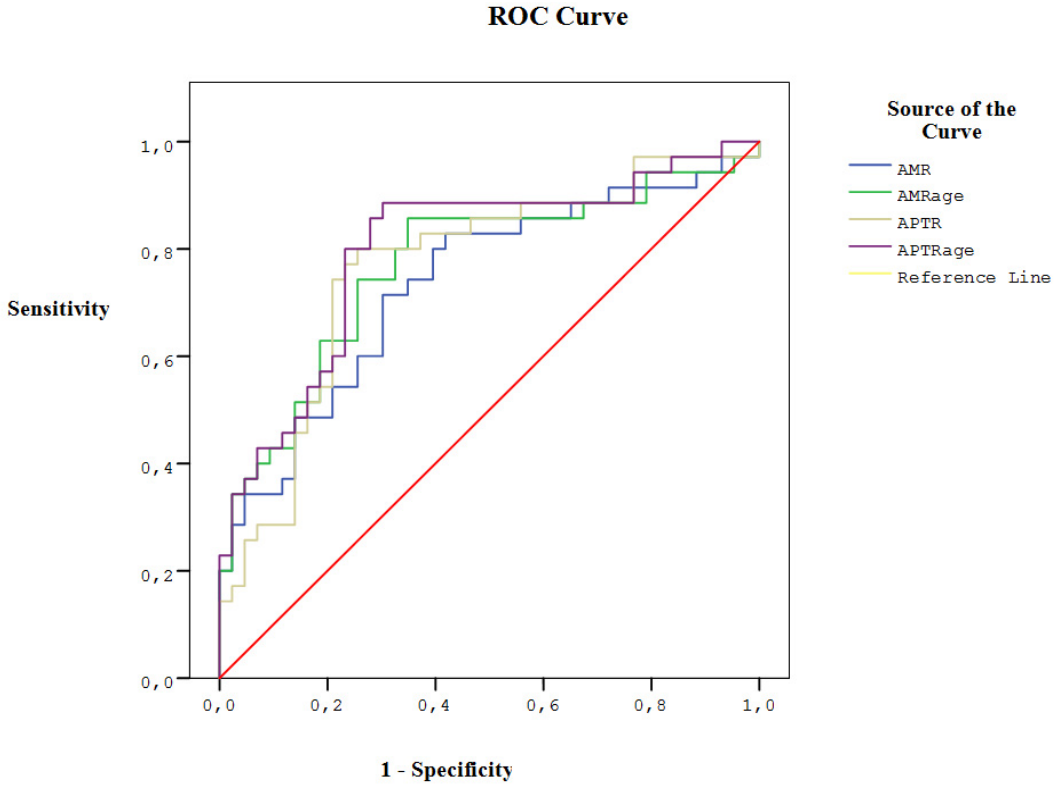

Figure 1. ROC curve analysis for AMR, APTR, AMRage and APTRage for predicting significiant fibrosis.

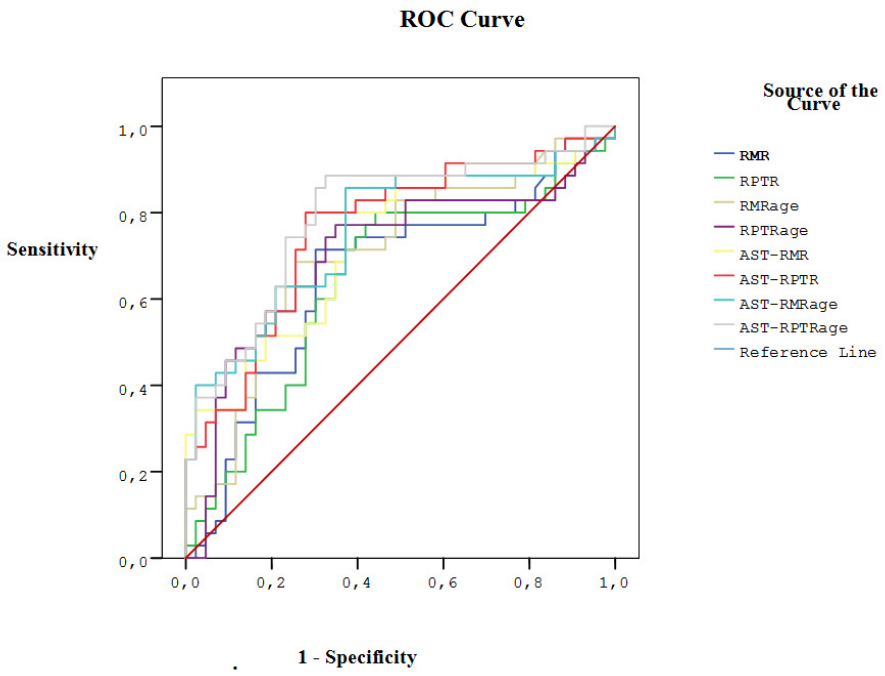

Figure 2. ROC curve analysis for RMR, RPTR, RMRage, RPTRage, AST-RMR, AST-RPTR, AST-RMRage and AST-RPTRage for predicting significiant fibrosis.

DISCUSSION

The patients enrolled in the study were male and generally young adult (23.95±5.42 years), since our centers are military hospital and our patients are usually young adult male patients and very small number women have been seen in our clinic. Hereby, as a drawback, our findings might not be generalizable to women. Besides, there were only 7 patients (9%) with fibrosis score 3 and there was no patient with fibrosis score 4 or cirrhosis. It has been evaluated that this may be due to the low age of HCV infection in our young adult patients.

In our cohort, there was no correlation between CBC parameters such as RDW, MPV, PDW, PCT, PLR, NLR, RPR and HCV RNA or HAI score and no difference in PLR and NLR between groups according to HAI scores or fibrosis scores. PLR and NLR have been shown to be associated with inflammation as well as with the severity of inflammation (23, 24). While there are studies suggested that NLR is related to fibrosis and disease severity in patients with non-alcoholic steatohepatitis (NASH), there are also studies showing that NLR is not associated with severity of hepatic inflammation and fibrosis in patients with non-alcoholic fatty liver disease (NAFLD) (17, 18). NLR has been also considered to evaluate disease prognosis in HCC (25). Furthermore, NLR has been reported to be negatively correlated with HAI score or to be correlated with HCV RNA levels or to be used as a novel non-invasive marker of fibrosis in chronic HBV patients (5, 19, 20). Also, PCT values have been shown to be inversely correlated with HBV deoxyribonucleic acid (DNA) levels (26). However, no difference in PLR and NLR values between groups according to HAI scores or fibrosis scores and no correlation between HCV RNA and PLR, MPV, PCT or PDW have been also indicated (10, 20).

In our study, there were difference only in MPV and PCT values between groups according to fibrosis score. MPV and PCT values were significiantly lower in patients with significiant fibrosis compared with no or minimal fibrosis group. However, there was no difference in all variables between HAI<7 group and HAI>6 group. In the literature, there are studies in which MPV values were evaluated between acute and chronic hepatitis B patients and healthy controls.

In these studies, no significant difference was found between healthy individuals and acute hepatitis B patients. On the other hand, it has been shown that chronic hepatitis B patients have higher MPV values than both healthy individuals and acute hepatitis B patients. (8, 11). Notwithstanding, the model of end-stage liver disease (MELD) score has been shown to be positively correlated with MPV. It has also been reported that MPV can be defined as an independent predictive factor in hepatic fibrosis (8, 11). However, elevation in MPV levels has been associated with severity of fibrosis, on the contrary, whereas no difference in MPV values between groups with different fibrosis degree or low levels of MPV as independent variables decretive the seriousness of fibrosis have been indicated (8-15). In addition, in a study investigating MPV levels in patients with HCV or HBV infection, reliable results were not found in hepatitis B groups. However, in patients with advanced liver injury with hepatitis C, MPV has been indicated as a useful predictor of liver injury (14).

There are also studies suggesting divergent findings about other platelet indices such as PDW and PCT in patients with chronic viral hepatitis. Higher PDW values in HCV patients with advanced fibrosis or high levels of PDW as independent variables decretive the seriousness of fibrosis in HBV patients or significiantly lower PCT values in HBV patients with cirrhosis or high fibrosis have been reported (13, 15, 16). Conversly, there are trials showing no significiant difference in PDW values or in PCT values between the groups according to fibrosis degree in HBV or HCV patients (8, 10).

As mentioned above, it is questionable whether platelet indices are useful as predictors of fibrosis severity. Because of the production of larger platelets via stimulation of megakaryocytes in consequence of the decrease of platelet counts, an inverse correlation between platelet size and platelet count is anticipated (14). Large platelet count increases in the presence of mild inflammation and decreases in severe inflammation. Therefore, while MPV values decrease as the severity of inflammation increases, it is thought to be valid in the opposite case. In addition, while MPV values decrease in hypoproliferative thrombocytopenia, they increase in destructive thrombocytopenia (27,28). So, MPV and the other platelet indices affected platelet sizes, namely PDW and PCT, may be defined as negative acute phase reactants in addition to acute phase reactants (27, 28). Consequently, it is a fact that not only platelet count but also platelet size indices such as MPV, PDW, PCT are influenced by severity of fibrosis, but also large-scale studies searching the role and the course of these platelet indices in viral hepatitis patients with different phases of fibrosis are required.

RDW and/or RPR values have been also shown to be related to fibrosis in patients with non-alcoholic steatohepatitis, primary biliary cirrhosis or primary viral hepatitis such as HBV or HCV infection, associated with severity (4-9, 21, 22). However, there was no difference in RDW or RPR values between groups with respect to fibrosis score or to HAI score in our study. Elevated RDW values have been shown to be indicators of inflammatory stress, and also, suppression of erythrocyte maturation by inflammatory cytokines, hypersplenism as a result of portal hypertension, affected hematopoiesis since decreased folic acid by nutritional deficiencies were described as possible mechanisms for elevated RDW values in patients with liver diseases (4, 29).

Since percutaneous liver biopsy has complications and drawbacks mentioned above, there is a need for non-invasive predictive models to foretell fibrosis degree in patients with viral hepatitis. Thus, indirect serum markers including AST, ALT, INR (International Normalized Ratio), age and platelet count have been evaluated in scoring systems such as AST-to-ALT ratio (AAR), AST-to-platelet ratio index (APRI) score, FIB-4 index (fibrosis index based on four factors), King's score, Lok index and Goteborg University Cirrhosis Index (GUCI) in some studies with questionable results (2, 3). These scoring systems are cheaper, consist of routinely used blood tests. In addition, as other benefits; While providing support to the patients who will be planned for outpatient treatment at the decision stage before starting the treatment, there is no need for special expertise and it allows more widespread use. However, the

scores are generally have been considered to be more important and useful to distinguish between severe fibrosis or cirrhosis and no or minimal fibrosis. Scoring to determine the severity of liver fibrosis has a wide range and the cut-off values cannot be clearly revealed are disadvantages. In addition, there is no clear data on sensitivity and specificity rates (2, 3, 30). Furthermore, this scoring system is negatively affected by the drugs used by the patient (warfarin, corticosteroids, etc.), the presence of a different focus of infection in the patient, chronic inflammatory and hematological diseases. Accordingly, we also investigated new scoring systems calculated using patients' serum AST levels, age, RDW, MPV and PCT levels to fortell significant fibrosis (fibrosis score ≥ 2). In the wake of our findings, we can say that CBC parameters including especially platelet indices (MPV, PCT) and/or RDW may be useful in scoring systems defining severity of fibrosis in treatment naive HCV patients, but, in order to highlight the accurate role and the cut-off values of these non-invasive scoring systems, double-blind randomized larger studies are needed.

There are several limitations in this study. First of all, most important one is the retrospective study. Besides, although the number of centers included in the study was two, the number of patients included in the study was small. Furthermore, as mentioned above, since our patients were male, our findings might not be generalizable to women. As another drawback, the number of patients with advanced fibrosis (fibrosis score ≥3) in the significant fibrosis group was limited due to the low infection age of HCV infection in our young adult patients, and there was no patient with cirrhosis. Finally, due to the retrospective nature of the study, the pathologists who performed the histopathological evaluation were different.

CONCLUSION

In our cohort, only MPV and PCT values were significiantly lower in patients with significiant fibrosis compared with the other group, while there was no difference in the other CBC parameters or ratios such as PLR, NLR and RPR between two groups. Moreover, there was no difference in all variables between groups according to HAI scores. We think that platelet indices including particularly MPV and PCT can be used in scoring systems defining severity of fibrosis in treatment naive HCV patients, but randomized large-scale studies including viral hepatitis patients with different phases of fibrosis are required.

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