Association between red cell distribution width-to-platelet ratio and hepatic fibrosis in nonalcoholic fatty liver disease

A cross-sectional study

Wen-Jie Zhou, MD<sup>ab</sup>, Jing Yang, MD<sup>b</sup>, Ge Zhang, MD, PhD<sup>b</sup>, Zheng-Qiang Hu, MD<sup>a</sup>, Yong-Mei Jiang, PhD<sup>a</sup>, Fan Yu, MD<sup>ab</sup>,∗

Abstract

**Background:** We aimed to assess the association between red cell distribution width-to-platelet ratio (RPR) and hepatic fibrosis in nonalcoholic fatty liver disease.

**Methods:** The 388 subjects fulfilling the diagnostic criteria of Nonalcoholic fatty liver disease (NAFLD) were enrolled in this cross-sectional study. Red cell distribution, platelet, and other clinical and laboratory parameters were measured.

**Results:** NAFLD patients with advanced fibrosis had significantly higher RPR than those without fibrosis (P < .001). Spearman correlation analysis showed that RPR were significantly correlated with age, sex, creatinine, hemoglobin, white blood cell, and advanced fibrosis (all with P < .05). Multivariate logistic regression analysis showed that RPR was an independent factor predicting advanced fibrosis (fibrosis-4 calculator ≥1.5) in NAFLD patients (OR: 5.718, 95% CI: 3.326-9.830, P < .001).

**Conclusions:** Our findings suggested that RPR were significantly associated with advanced fibrosis in nonalcoholic fatty liver disease patients.

**Abbreviations:** γ-GT = γ-glutamyltransferase, ALT = alanine aminotransferase, AST = aspartate aminotransferase, BMI = Body Mass Index, Cr = creatinine, CRP = C-reactive protein, DBP = diastolic blood pressure, DM = diabetic mellitus, FIB-4 = fibrosis-4 calculator, FPG = fasting plasma glucose, HDL-c = high-density lipoprotein cholesterol, Hgb = hemoglobin, LDL-c = low-density lipoprotein cholesterol, NAFLD = nonalcoholic fatty liver disease, NASH = nonalcoholic steatohepatitis, PLT = platelet, RDW = red cell distribution width, RPR = red cell distribution width-to-platelet ratio, SBP = systolic blood pressure, Tch = total cholesterol, TG = triglycerides, WBC = white blood cell.

**Keywords:** advanced fibrosis, fibrosis-4 calculator, nonalcoholic fatty liver disease, red cell distribution width-to-platelet ratio

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) has recently been recognized as a major public health problem, the prevalence of NAFLD varies from 20% to 51%, depending on the study population in China over the past few decades. The broad spectrum of NAFLD diseases ranges from simple liver steatosis to nonalcoholic steatohepatitis (NASH) and advanced fibrosis and cirrhosis. Only a minority of individuals, those with NASH, are prone to the risk of fibrosis and cirrhosis. Compared with these invasive tests to diagnosis NAFLD, we used the noninvasive ultrasound technique, in our study, which has high sensitivity and specificity in detecting steatosis and fibrosis.

Red blood cell distribution width (RDW) is a measure of variability of erythrocyte size in peripheral blood (i.e., anisocytosis). In recent past, RDW has gained substantial attention as a prognostic marker of various medical conditions, such as sepsis, acute myocardial infarction, heart failure, autoimmune diseases, liver diseases, and various malignancies. Some studies found elevated RDW was independently associated with advanced fibrosis in NAFLD, RDW was higher in the severe inflammation group in non-alcoholic steatohepatitis and can be used as an indicator in non-alcoholic steatohepatitis patients with high sensitivity and specificity.

Platelet (PLT) count is decreased in liver diseases has long been known. The utility of PLT count stems from the observations in liver cirrhosis and pathophysiologic changes which occur including splenomegaly and sequestration of PLT. Several studies have found the platelet count to be an independent predictor of liver cirrhosis, fibrosis severity (grade) in NAFLD, and nonalcoholic steatohepatitis (NASH). Moreover, PLT...
count has been included in some NAFLD fibrosis scoring systems for adults, such as APRI, FIB-4, King, Lok, FI, Forns, and Fibro Index scores.[17–21]

Therefore, the platelet count and RDW are ideal biomarkers of the severity of fibrosis in NAFLD patients. RDW-to-platelet ratio (PRR) will enhance this function. In recent past, PRR has gained substantial attention as a prognostic marker of various medical conditions such as severe burn injury, primary biliary cholangitis, patent ductus arteriosus, predicting hepatic fibrosis and cirrhosis in chronic hepatitis B, diagnosis of premature ovarian insufficiency; myocardial infarction; acute pancreatitis in pregnancy.[18,19,22–27] Because it is simple, easy to measure and handle, cost-effective, and accurate for predicting the severity of fibrosis, we plan to research the association between PRR and the level of fibrosis in NAFLD.

2. Materials and methods

2.1. Patients

This study included 485 participants who underwent individual health examinations that included a physical examination and clinical laboratory tests at the West China Second University Hospital between May and October 2017, and were diagnosed with fatty liver. All participants underwent anthropometric and biochemical parameter analyses. Patients were excluded if they exhibited any of the following conditions: drinkers (alcohol consumption >140 g/week for men and >70 g/week for women were categorized as drinkers, n=46), viral hepatitis (n=35), chronic liver disease (n=5), renal insufficiency (n=3), cancer (n=2), elevated tumor markers (n=3), pregnancy (n=1), and recent infection (n=2). The remaining 388 participants (301 men and 87 women) were enrolled in the study. Informed consent was obtained from all participants and the study was approved by the ethics committee of the West China Second University Hospital, Sichuan University.

2.2. Clinical laboratory and anthropometric parameters

Weight, height, and blood pressure (systolic blood pressure SBP; diastolic blood pressure DBP) were measured, and Body Mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared. RDW to platelet ratio (RPR)=RDW/100/PLT(10^9/L). FIB-4 index was calculated according to the following equation[19]:

\[ \text{FIB-4} = \frac{ALT}{AST} \times \sqrt{\frac{APRI}{PLT}} \]

The clinical examinations were conducted in the morning after an overnight fast. RDW, hemoglobin (Hgb) level, PLT, and white blood cells (WBC) were determined using the XE-2100 automated hematology analyzer (Sysmex Corp, Kobe, Japan). Alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyltransferase (γ-GT), triglycerides (TG), total cholesterol (Tch), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), high-sensitivity C-reactive protein (CRP), fasting plasma glucose (FPG), and creatinine (Cr) were assessed using an automatic biochemical analyzer (Hitachi 7600; Hitachi, Tokyo, Japan) with Roche reagents (Roche Diagnostics, GmbH, Mannheim, Germany).

2.3. Diagnostic criteria for NAFLD

Liver ultrasound examinations were performed by experienced radiologists who were unaware of the clinical and laboratory data, using a Toshiba Nemio 20 sonography machine with a 3.5-MHz probe (Toshiba, Tokyo, Japan). Liver ultrasound examinations was used to define NAFLD patients. Hepatic steatosis was diagnosed according to the guidelines established for the diagnosis and treatment of NAFLD issued by the Fatty Liver Disease Study Group of the Chinese Liver Disease Association.[28] Specifically, hepatic steatosis was diagnosed according to characteristic echo patterns, such as diffuse hyperechogenicity of the liver relative to the kidneys, ultrasound beam attenuation, and poor visualization of intrahepatic structures. Liver ultrasound examinations were performed by a single experienced radiologist blinded to the clinical and laboratory data.

We used the fibrosis-4 calculator (FIB-4) index for evaluating advanced fibrosis (FIB-4 ≥1.3) of NAFLD according to the study of Xun et al.[29] Although slightly less accurate than liver biopsy, FIB-4 index can reliably indicate advanced fibrosis in Chinese NAFLD patients.[29]

2.4. Statistical analyses

Statistical analyses were performed using SPSS version 16 (SPSS, Chicago, IL). Data that were normally distributed are reported as mean±standard deviation and data that had a skewed distribution are reported as median and range. Differences between 2 groups were analyzed using the Student t test or the Mann–Whitney U test. Differences among multi-groups were analyzed using one-way analysis of variance or the Kruskal–Walls H test. Spearman correlation analysis was used to examine correlations between PRR and clinical and laboratory parameters. Univariable and multivariable logistic regression was used to examine associations between PRR and NAFLD participants. All statistical tests were two-tailed and a P value<.05 was considered statistically significant.

3. Results

3.1. Clinical characteristics of participants

The demographic and biochemical characteristics of study participants were shown in Table 1. There were 388 NAFLD participants included in the study and 74 (19.1%) NAFLD participants with advanced fibrosis. NAFLD with and without advanced fibrosis had significant differences in SBP, ALT, PLT, FPG, WBC, RDW, and prevalence of diabetic mellitus (DM). We referred to the study of Chen et al that devised the RDW to platelet ratio (PRR) to amplify the difference in the RDW and platelets among patients with different fibrosis stages. In Table 1, NAFLD with advanced fibrosis had significant higher RPR than NAFLD without advanced fibrosis [7.03 (3.58–12.86) vs 5.48 (3.23–11.22), P<.001].

3.2. Association between PRR and various parameters in NAFLD participants

Our results show that PRR were significantly correlated with age (r=.157, P=.002), sex (r=-.132, P=.009), Cr (r=.136, P=.007), Hgb (r=.155, P=.002), WBC (r=-.250, P<.001), and advanced fibrosis (r=.440, P<.001) (shown in Table 2). The study of Chen et al[17] observed that PRR can predict significant
fibrosis in chronic hepatitis B patients with relatively high accuracy, to get a further research of the association between RPR and advanced fibrosis in NAFLD participants, we used univariate logistic regression and multivariate logistic regression with forward selection to analyze the odds and P values. The results of Univariate and multivariate logistic regression models were shown in Table 3. We put age, sex, SBP, DBP, BMI, ALT, AST, γ-GT, TG, Cr, Tch, HDL-C, FPG, CRP, Hgb, PLT, RDW, RPR, and DM prevalence into the univariate logistic regression analysis, and we found age, SBP, AST, FPG, RPR, and DM prevalence were significantly correlated with advanced fibrosis (all P < .05). Then, we put age, SBP, AST, FPG, RPR, and DM prevalence into multivariate logistic regression with forward selection, and found age, AST, and RPR were significantly associated with advanced fibrosis (all P < .05). This result suggested that RPR (OR: 5.718, 95% CI: 3.326–9.830, P < .001) was an independent factor for advanced fibrosis prediction in NAFLD participants.

3.3. Optimizing the predictive model for advanced fibrosis

To form a more practical model for predicting NAFLD advanced fibrosis, we put age, AST, and RPR screened by the multivariate logistic regression into the new model. The new model is presented as logit (N index) = 0.307 × age + 0.149 × AST + 1.685 × RPR – 32.124. Furthermore, we applied a ROC curve to test the sensitivity and specificity of this new predictive model (Fig. 1). The area under curve (AUC) of new model was 0.976 with the 95% confidence interval from 0.964 to 0.988, the sensitivity and specificity of which were 98.7% and 87.3%. The AUC of RPR was 0.816 with the 95% confidence interval from 0.765 to 0.868, the cutoff value was 6.39, the sensitivity and the specificity were 74.3% and 79.3%. The AUC of new model was significantly larger than AUC of RPR, z statistic was 6.193, P < .001.

4. Discussion

In the current study from NAFLD population, we provided evidence that NAFLD with advanced fibrosis had a higher RPR. The results also indicated that RPR ratio was an independent risk factor for advanced fibrosis. Finally, we established a predictive model for NAFLD by utilizing age, AST, and RPR with a larger AUC, high sensitivity and specificity. Our study is the first to demonstrate a significant association between RPR and NAFLD

| Table 1 | Characteristics of the NAFLD patients with and without advanced fibrosis. |
|---------|---------------------------------------------------------------------|
| Variable | Without advanced fibrosis (314) | with advanced fibrosis (74) | P value |
| Age (yr) | 42.2 ± 9.6 | 58.9 ± 10.5 | <.001 |
| Sex (F/M) | 68/246 | 19/55 | .456 |
| Body mass index (kg/m²) | 25.2 ± 2.7 | 26.0 ± 2.3 | .659 |
| Systolic blood pressure (mmHg) | 130 ± 16 | 138 ± 19 | <.001 |
| Diastolic blood pressure (mmHg) | 80 ± 11 | 83 ± 11 | .085 |
| Alanine aminotransferase (U/L) | 29 (11–1184) | 26 (7–164) | .034 |
| Aspartate aminotransferase (U/L) | 23 (14–87) | 26 (13–101) | .006 |
| Glutamyltransferase (U/L) | 34 (7–97) | 33 (11–98) | .333 |
| Triglyceride (mmol/L) | 1.66 (0.34–21.05) | 1.55 (0.53–10.91) | .647 |
| Creatinine (mmol/L) | 7.25 ± 13.7 | 71.9 ± 14.0 | .734 |
| Total cholesterol (mmol/L) | 4.95 ± 1.00 | 5.11 ± 0.93 | .213 |
| High-density lipoprotein cholesterol (mmol/L) | 1.12 ± 0.26 | 1.17 ± 0.26 | .145 |
| Low-density lipoprotein cholesterol (mmol/L) | 2.67 ± 0.58 | 2.76 ± 0.68 | .286 |
| Fasting plasma glucose (mmol/L) | 5.23 (3.95–12.42) | 6.07 (4.27–16.46) | .003 |
| Uric acid (mmol/L) | 372 (146–570) | 349 (231–538) | .057 |
| High-sensitivity C-reactive protein (mg/L) | 1.5 (0.3–11.7) | 1.5 (0.4–10.9) | .386 |
| Hemoglobin (g/L) | 155 ± 12 | 152 ± 12 | .524 |
| Platelet (10³/μL) | 240 ± 47 | 186 ± 44 | <.001 |
| White blood cells (10³/μL) | 6.6 (3.7–11.4) | 6.3 (3.9–9.1) | .014 |
| Red blood cell distribution width | 13.04 ± 0.71 | 13.24 ± 0.73 | .036 |
| RDW × 100/PLT | 5.48 (3.23–11.22) | 7.03 (3.58–12.86) | <.001 |
| DM prevalence (%) | 29.3 | 47.3 | <.001 |

DM = diabetic mellitus, NAFLD = nonalcoholic fatty liver disease, RDW = red cell distribution width.

| Table 2 | The correlation between RPR and various parameters. |
|---------|--------------------------------------------------|
| Variables | r | P value |
| Age (yr) | 0.157 | .002 |
| Sex (F/M) | −0.132 | .000 |
| Body mass index (kg/m²) | 0.015 | .763 |
| Systolic blood pressure (mmHg) | 0.050 | .329 |
| Diastolic blood pressure (mmHg) | 0.029 | .565 |
| Alanine aminotransferase (U/L) | 0.021 | .678 |
| Aspartate aminotransferase (U/L) | 0.009 | .050 |
| Glutamyltransferase (U/L) | 0.025 | .625 |
| Triglyceride (mmol/L) | −0.003 | .949 |
| Creatinine (mmol/L) | 0.136 | .007 |
| Total cholesterol (mmol/L) | 0.024 | .642 |
| High-density lipoprotein cholesterol (mmol/L) | −0.015 | .765 |
| Low-density lipoprotein cholesterol (mmol/L) | 0.028 | .397 |
| Fasting plasma glucose (mmol/L) | 0.026 | .566 |
| Uric acid (mmol/L) | −0.006 | .900 |
| High-sensitivity C-reactive protein (mg/L) | −0.087 | .086 |
| Hemoglobin (g/L) | 0.155 | .002 |
| White blood cells (10³/μL) | −0.250 | <.001 |
| DM prevalence (%) | 0.025 | .628 |
| Advanced fibrosis | 0.440 | <.001 |

DM = diabetic mellitus, RPR = red cell distribution width to-platelet ratio.
| Variables                        | Univariate OR (95CI) | P value | Multivariate OR (95CI) | P value |
|---------------------------------|----------------------|---------|------------------------|---------|
| Age (yr)                        | 1.171 (1.128–1.214)  | <.001   | 1.378 (1.259–1.509)    | <.001   |
| Sex (F/M)                       | 0.800 (0.445–1.439)  | .456    |                        |         |
| Body mass index (kg/m²)         | 0.978 (0.887–1.078)  | <.058   |                        |         |
| Systolic blood pressure (mmHg)  | 1.028 (1.012–1.044)  | <.001   | 0.998 (0.971–1.026)    | .890    |
| Diastolic blood pressure (mmHg) | 1.020 (0.997–1.044)  | .068    |                        |         |
| Alanine aminotransferase (U/L)  | 0.990 (0.977–1.005)  | .183    |                        |         |
| Aspartate aminotransferase (U/L)| 1.036 (1.009–1.063)  | .007    | 1.170 (1.103–1.241)    | <.001   |
| Glutamyltransferase (U/L)       | 0.991 (0.978–1.005)  | .216    |                        |         |
| Triglyceride (mmol/L)           | 1.016 (0.982–1.050)  | .825    |                        |         |
| Creatinine (mmol/L)             | 0.997 (0.979–1.015)  | .753    |                        |         |
| Total cholesterol (mmol/L)      | 1.164 (0.915–1.481)  | .216    |                        |         |
| High-density lipoprotein cholesterol (mmol/L) | 1.981 (0.787–4.986)  | .147    |                        |         |
| Low-density lipoprotein cholesterol (mmol/L) | 1.255 (0.827–1.904)  | .286    |                        |         |
| Fasting plasma glucose (mmol/L) | 1.352 (1.120–1.631)  | .002    | 1.253 (0.906–1.733)    | .173    |
| Uric acid (µmol/L)              | 0.997 (0.993–1.000)  | .558    |                        |         |
| High-sensitivity C-reactive protein (mg/L) | 0.970 (0.843–1.115)  | .666    |                        |         |
| Hemoglobin (g/L)                | 0.982 (0.962–1.003)  | .086    |                        |         |
| Platelet (10^12/L)              | 0.972 (0.965–0.980)  | <.001   |                        |         |
| White blood cells (10^9/L)      | 0.781 (0.642–0.949)  | .013    |                        |         |
| Red blood cell distribution width | 1.400 (1.004–1.952)  | .047    |                        |         |
| RDW×100/PLT                     | 2.194 (1.791–2.699)  | <.001   | 5.718 (3.326–9.830)    | <.001   |
| DM prevalence (%)               | 2.166 (1.291–3.632)  | .003    | 0.454 (0.136–1.507)    | .197    |

DM = diabetic mellitus, NAFLD = nonalcoholic fatty liver disease, PLT = platelet, RDW = red cell distribution width.

Figure 1. The ROC curve of this new predictive model.
with advanced fibrosis. NAFLD is reported to be associated with genetic, environmental, and metabolic factors. The underlying mechanism by which RPR interacts with NAFLD remained unclear.

Some studies suggested that serum RDW and PLT were associated with liver fibrosis and cirrhosis.\(^{[14,15]}\) The RDW is an indicator of the variability of the circulating RBC size and often used to diagnose different types of anemia.\(^{[17]}\) Recent studies indicated that a higher RDW was associated with a poor survival in gastric cancer, lung disease, ovarian cancers, hepatocellular carcinoma, and fatty liver disease.\(^{[32]}\) RDW may represent an easily obtainable and inexpensive prognostic marker in various patient populations. Chen et al.\(^{[19]}\) found that hemoglobin, RDW, and platelets were independent predictors of the liver fibrosis stage in patients with chronic hepatic B. Another study by Lou et al.\(^{[34]}\) found that higher RDW values were associated with disease severity in patients with hepatitis B. PLT count was decreased in liver diseases has long been known, and some studies reported a significant linear decrease in PLT count accompanied with the histological severity of fibrosis in NAFLD worsened.\(^{[12,16,20,35]}\) The platelet count has been used in the most predictive models for liver fibrosis and cirrhosis, such as NAFLD fibrosis score, Fibrosis-4 calculator (FIB-4), AST/ALT ratio, and diabetes score, and AST-to-platelet ratio index. These scores have been used to detect fibrosis and cirrhosis in adult patients with hepatitis B and C, alcoholic liver disease and nonalcoholic fatty liver disease with platelet count decreased.\(^{[21,36]}\)

Liver fibrosis is the result of excessive accumulation of extracellular matrix components, which consist of collagen and other components.\(^{[17]}\) The development of liver fibrosis is considered to be a complex trait. The role of platelets in the progression of fibrosis is not well understood. Lin et al.\(^{[37]}\) and Iwasaki et al.\(^{[38]}\) designed to investigate whether platelets could reduce liver fibrosis and promote liver regeneration in fibrotic liver and found that platelets degraded extracellular matrix and reduced liver fibrosis by decreasing expression of TGF-b, and increasing expression of MMP-9, in addition to promoting liver regeneration. Additionally, the mechanism underlying the association between the RDW and the progression of fibrosis is also not well understood. Lippi et al.\(^{[39]}\) speculated that the association between RDW and inflammatory states was simply an epiphenomenon of underlying abnormal iron metabolism and/or anemia. Lan et al.\(^{[40]}\) found RDW values were increased and were related with various biomarkers and MELD grades in liver disease, and RDW could be used as an inflammatory marker for predicting chronic hepatitis B, liver cirrhosis, and hepatocellular carcinoma when combined with Hgb, AST, γ-GT, alkaline phosphatase, and globulin. Fujita et al.\(^{[41]}\) indicated iron overload was considered a putative element that interacts with oxygen radicals in inducing liver fibrosis and insulin resistance, and may have a role in the pathogenesis of NASH. However, some studies suggest that the use of Waist Circumference as a parameter of Metabolic Syndrome.\(^{[5]}\) there were few evidences to prove it in Chinese population so far.

This study has some limitations. First, because this is a retrospectively cross-sectional study, the present analysis is limited in its ability to establish causal or temporal relationships between RPR and liver fibrosis. Due to the lack of data, we did not investigate the possible causes that may affect RDW values, such as iron or vitamin B12 deficiency. Second, the diagnosis of NAFLD was based on ultrasonography examination. Although ultrasonography is widely used in epidemiological studies of NAFLD, ultrasonography is not sensitive enough to detect mild steatosis. Third, we used the FIB-4 index for evaluating advanced fibrosis of NAFLD according to the studies of Xun et al.\(^{[29]}\) FIB-4 index was not sensitive enough to identify patients with a mild degree of fibrosis who are at risk of progression. Finally, this study involved a single center and have posed a selection bias. Therefore, the performance of the RPR should be further confirmed in multi-center designed studies.

5. Conclusions

In conclusion, our results demonstrate a significant correlation between RPR and advanced fibrosis in NAFLD population. Because RDW and platelet values are easily available at no additional cost and are highly reproducible, RPR may serve as an important marker and potentially reduce the need for liver biopsy in NAFLD population. Further research on the involvement of RPR in NAFLD will enhance our understanding of the development of fibrosis, and benefit in the eventual development of new prevention and treatment strategies for NAFLD.

Acknowledgments

The authors gratefully acknowledge the staff of the Department of Laboratory Medicine of West China Second Hospital of Sichuan University for collecting data and blood samples.

Author contributions

Conceptualization: Zheng-Qiang Hu, Yong-Mei Jiang, Fan Yu.
Data curation: Jing Yang, Zheng-Qiang Hu.
Investigation: Jing Yang.
Project administration: Zheng-Qiang Hu, Fan Yu.
Software: Ge Zhang.
Supervision: Ge Zhang.
Writing – original draft: Wen-Jie Zhou.
Writing – review & editing: Wen-Jie Zhou, Zheng-Qiang Hu, Fan Yu.

References

[1] Fan JG. Epidemiology of alcoholic and nonalcoholic fatty liver disease in China. J Gastroenterol Hepatol 2013;28(Suppl 1):11–7.
[2] Liu F, Zhou H, Cao L, et al. Risk of reduced platelet counts in patients with nonalcoholic fatty liver disease (NAFLD): a prospective cohort study. Lipids Health Dis 2018;17:221.
[3] Alkhouri N, McCullough AJ. Noninvasive diagnosis of NASH and liver fibrosis within the spectrum of NAFLD. Gastroenterol Hepatol (N Y) 2012;8:661–8.
[4] Stefan N, Haring HU, Cusi K. Non-alcoholic fatty liver disease: causes, diagnosis, cardiometabolic consequences, and treatment strategies. Lancet Diabetes Endocrinol 2019;7:313–24.
[5] Fatrahi MR, Niknam R, Safarpoor A, et al. The prevalence of metabolic syndrome in non-alcoholic fatty liver disease; a population-based study. Middle East J Dig Dis 2016;8:131–7.
[6] Alizadeh A, Mansour-Ghanaei F, Rooodzar A, et al. Laboratory tests, liver vessels color doppler sonography, and fibrosis can in patients with nonalcoholic fatty liver disease: an observation study. J Clin Imaging Sci 2018;8:12.
[7] Farkas N, Szabo A, Lorand V, et al. Clinical usefulness of measuring red blood cell distribution width in patients with systemic sclerosis. Rheumatol (Oxford) 2014;53:1439–45.
[8] Han YQ, Zhang L, Yan L, et al. Red blood cell distribution width predicts long-term outcomes in sepsis patients admitted to the intensive care unit. Clin Chim Acta 2018;487:112–6.
[9] Ilhan E, Guvenc TS, Altay S, et al. Predictive value of red cell distribution width in intrahospital mortality and postintervention thrombolysis in myocardial infarction flow in patients with acute anterior myocardial infarction. Coron Artery Dis 2012;23:430–4.
[10] Zeng T, Yu J, Tan L, et al. Noninvasive indices for monitoring disease course in Chinese patients with autoimmune hepatitis. Clin Chim Acta 2018;486:135–41.
[11] Fan X, Deng H, Wang X, et al. Association of red blood cell distribution width with severity of hepatitis B virus-related liver diseases. Clin Chim Acta 2018;482:155–60.
[12] Muhlestein JB, Lappe DL, Anderson JL, et al. Both initial red cell distribution width and change in RDW during heart failure hospitalization are associated with length of hospital stay and 30-day outcomes. Int J Lab Hematol 2016;38:328–37.
[13] Ai L, Mu S, Hu Y. Prognostic role of RDW in hematological malignancies: a systematic review and meta-analysis. Cancer Cell Int 2018;18:61.
[14] Kim HM, Kim BS, Cho YK, et al. Elevated red cell distribution width is associated with advanced fibrosis in NAFLD. Clin Mol Hepatol 2015;19:258–65.
[15] Iida H, Kaibori M, Matsui K, et al. Ratio of mean platelet volume to platelet count is a potential surrogate marker predicting liver cirrhosis. World J Hepatol 2018;10:82–7.
[16] Chen XL, Chen TW, Zhang XM, et al. Platelet count combined with right liver volume and spleen volume measured by magnetic resonance imaging for identifying cirrhosis and esophageal varices. World J Gastroenterol 2015;21:10184–91.
[17] Kayadibi H, Yasar B, Ozkara S, et al. The diagnostic accuracy of the Forns index, platelet count and AST to Platelet Ratio Index derived fibrosis index for the prediction of Hepatitis C virus-related significant liver fibrosis and cirrhosis. Scand J Clin Lab Invest 2014;74:240–7.
[18] Taef A, Huang CC, Kolli K, et al. Red cell distribution width to platelet ratio, a useful indicator of liver fibrosis in chronic hepatitis patients. Hepatol Int 2015;9:454–60.
[19] Chen B, Ye B, Zhang J, et al. RDW to platelet ratio: a novel noninvasive index for predicting hepatic fibrosis and cirrhosis in chronic hepatitis B. PLoS One 2013;8:e67880.
[20] Iro T, Ishigami M, Ishizu Y, et al. Utility and limitations of noninvasive fibrosis markers for predicting prognosis in biopsy-proven Japanese non-alcoholic fatty liver disease patients. J Gastroenterol Hepatol 2018;34:207–14.
[21] Deng H, Qi X, Guo X. Diagnostic accuracy of APRI, AAR, FIB-4, FI, King, Lok, Forns, and FibroIndex scores in predicting the presence of esophageal varices in liver cirrhosis: a systematic review and meta-analysis. Medicine (Baltimore) 2015;94:e1795.
[22] Pusuroglu H, Cakmak HA, Akgul O, et al. The prognostic value of admission red cell distribution width-to-platelet ratio in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Rev Port Cardiol 2015;34:597–606.
[23] Ilhan M, Ilhan G, Gok AF, et al. Evaluation of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and red blood cell distribution width-platelet ratio as early predictor of acute pancreatitis in pregnancy. J Matern Fetal Neonatal Med 2016;29:1476–80.
[24] Qiu L, Chen C, Li SJ, et al. Prognostic values of red blood cell distribution width, platelet count, and red cell distribution width-to-platelet ratio for severe burn injury. Sci Rep 2017;7:13720.
[25] Jiang X, Wang Y, Su Z, et al. Red blood cell distribution width to platelet ratio levels in assessment of histologic severity in patients with primary biliary cholangitis. Scand J Clin Lab Invest 2018;78:258–63.
[26] Ozer Bekmez B, Tayman C, Buyuktyacli M, et al. A promising, novel index in the diagnosis and follow-up of patent ductus arteriosus: Red cell distribution width-to-platelet ratio. J Clin Lab Anal 2018;22:616.
[27] Ilhan G, Atmaca FFV, Altan E, et al. Evaluation of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and red blood cell distribution width-platelet ratio for diagnosis of premature ovarian insufficiency. J Family Reprod Health 2016;10:211–6.
[28] Zeng MD, Fan JG, Lu LG, et al. Guidelines for the diagnosis and treatment of nonalcoholic fatty liver diseases. J Dig Dis 2008;9:108–12.
[29] Xun YH, Fan JG, Zang GQ, et al. Suboptimal performance of simple noninvasive tests for advanced fibrosis in Chinese patients with nonalcoholic fatty liver disease. J Dig Dis 2012;13:588–95.
[30] Zhou D, Wu Y, Lin Z, et al. Prognostic value of combination of pretreatment red cell distribution width and neutrophil-to-lymphocyte ratio in patients with gastric cancer. Gastroenterol Res Pract 2018;2018:8042388.
[31] Kalemcı S, Akin F, Sarıhan A, et al. The relationship between hematological parameters and the severity level of chronic obstructive lung disease. Pol Arch Intern Med 2018;128:171–7.
[32] Qin Y, Wang P, Huang Z, et al. The value of red cell distribution width in patients with ovarian cancer. Medicine (Baltimore) 2017;96:e6752.
[33] Zhao T, Cui L, Li A. The significance of RDW in patients with hepatocellular carcinoma after radical resection. Cancer Biomark 2016;16:507–12.
[34] Lou Y, Wang M, Mao W. Clinical usefulness of measuring red blood cell distribution width in patients with hepatitis B. PLoS One 2012;7:e37644.
[35] Jorgensen B, Fischer E, Ingeberg S, et al. Decreased blood platelet volume and count in patients with liver disease. Scand J Gastroenterol 1984;19:492–6.
[36] Petta S, Wong VW, Camma C, et al. Serial combination of non-invasive tools improves the diagnostic accuracy of severe liver fibrosis in patients with NAFLD. Aliment Pharmacol Ther 2017;46:617–27.
[37] Lin YL, Lin HW, Chen YC, et al. Hepatoprotective effects of naturally fermented noni juice against thioacetamide-induced liver fibrosis in rats. J Chin Med Assoc 2017;80:212–21.
[38] Iwasaki A, Sakai K, Moriya K, et al. Molecular mechanism responsible for fibronectin-controlled alterations in matrix stiffness in advanced chronic liver fibrogenesis. J Biol Chem 2016;291:72–88.
[39] Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009;133:628–32.
[40] Lan F, Wei H, Zhu X, et al. Increased red cell distribution width is strong inflammatory marker of liver diseases in a Guangxi population. Clin Lab 2017;63:389–98.
[41] Fujita N, Takei Y. Iron overload in nonalcoholic steatohepatitis. Adv Clin Chem 2011;55:103–32.