Retrospective Study

Value of gamma-glutamyltranspeptidase-to-platelet ratio in diagnosis of hepatic fibrosis in patients with chronic hepatitis B

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Abstract

AIM
To investigate the value of the gamma-glutamyltranspeptidase (GGT)-to-platelet (PLT) ratio (GPR) in the diagnosis of hepatic fibrosis in patients with chronic hepatitis B (CHB).

METHODS
We included 390 untreated CHB patients in this study. The GPR, aspartate aminotransferase (AST)-to-PLT ratio index (APRI), and fibrosis-4 (FIB-4) of all patients were analysed to determine if these parameter were correlated with age, gender, medical history, liver function (total bilirubin (TBil), alanine aminotransferase (ALT), and AST), GGT, PLT count, or hepatic fibrosis stage. The GPR, APRI, and FIB-4, as well as the combination of the GPR and APRI or the GPR and FIB-4 were assessed in different cirrhosis stages using receiver operating characteristic (ROC) curve analysis to evaluate their value in diagnosing hepatic fibrosis in CHB patients.

RESULTS
The GPR, APRI, and FIB-4 were not correlated with...
CHB patients’ age, gender, or disease duration ($P > 0.05$), but all of these parameters were positively correlated with serum ALT, AST, GGT, and PLT count ($P < 0.01$). Additionally, the GPR, APRI, and FIB-4 were positively correlated with hepatic fibrosis ($P < 0.01$); the areas under the ROC curve for the GPR in F1, F2, F3, and F4 stages were 0.723, 0.741, 0.826, and 0.833, respectively, which were significantly higher than the respective values for the FIB-4 and APRI (F1: 0.581, 0.612; F2: 0.706, 0.711; F3: 0.73, 0.751; and F4: 0.799, 0.778). The respective diagnostic cut-off points for each stage were 0.402, 0.448, 0.548, and 0.833, respectively. The diagnostic sensitivity and specificity were, respectively, 88.8% and 87.5% in F1, 72.7% and 89.7% in F2, 81.3% and 98.6% in F3, and 80% and 97.4% in F4 when the GPR and APRI were connected in parallel; 86.6% and 90.2%, 78.4% and 96%, 78.6% and 97.4%, and 73.2% and 97.9%, respectively, when the GPR and APRI were connected in series; 80.2% and 89%, 65% and 89%, 70.3% and 98.5%, and 78.8% and 96.8%, respectively, when the GPR and FIB-4 were connected in parallel; and 83.6% and 87.9%, 76.8% and 96.6%, 72.7% and 98%, and 74.4% and 97.7%, respectively, when the GPR and FIB-4 were connected in series.

**CONCLUSION**

The GPR, as a serum diagnostic index of liver fibrosis, is more accurate, sensitive, and easy to use than the FIB-4 and APRI, and the GPR can significantly improve the sensitivity and specificity of hepatic fibrosis diagnosis in CHB when combined with the FIB-4 or APRI.

**Key words:** Gamma-glutamyltraspeptidase-to-platelet ratio; APRI; FIB-4; Chronic hepatitis B; Hepatic fibrosis

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**Core tip:** Hepatic fibrosis is a precursor of cirrhosis for chronic hepatitis B patients. Severe hepatic fibrosis and cirrhosis can increase the incidence and mortality of primary liver cancer. Although liver biopsy is still the gold standard for the diagnosis of liver fibrosis, it is not widely used as a routine examination because of its invasiveness, high cost, and lack of repeatability. The aspartate aminotransferase (AST)-to-platelet (PLT) ratio index (APRI) and fibrosis-4 (FIB-4) are commonly used in the clinic as two noninvasive serum models; but their complicated calculation, poor sensitivity, and requirement for combination with other indexes for comprehensive evaluation of the degree of hepatic fibrosis actually increase the workload. As an alternative, transient elastography (Fibroscan) by imaging is considered a good tool for the diagnosis of hepatic fibrosis, but its performance is restricted by several factors, such as diet, obesity, ascites, and rib gap width. In recent years, researchers have tried to identify a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level, which could assist in early diagnosis to achieve timely treatment, delay cirrhosis or liver cancer incidence, improve patients’ quality of life, and prolong patients’ survival time.

Hepatic fibrosis is a precursor of cirrhosis in patients with chronic hepatitis B (CHB)\[1\]. Severe hepatic fibrosis and cirrhosis can increase the incidence and mortality of primary liver cancer\[2\]. Although liver biopsy is still the gold standard for the diagnosis of liver fibrosis, it is not widely used as a routine examination because of its invasiveness, high cost, and lack of repeatability. Aspartate aminotransferase (AST)-to-platelet (PLT) ratio index (APRI) and fibrosis-4 (FIB-4) are commonly used in the clinic as two noninvasive serum models; but their complicated calculation, poor sensitivity, and requirement for combination with other indexes for comprehensive evaluation of the degree of hepatic fibrosis actually increase the workload. As an alternative, transient elastography (Fibroscan) by imaging is considered a good tool for the diagnosis of hepatic fibrosis, but its performance is restricted by several factors, such as diet, obesity, ascites, and rib gap width. In recent years, researchers have tried to identify a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level, which could assist in early diagnosis to achieve timely treatment, delay cirrhosis or liver cancer incidence, improve patients’ quality of life, and prolong patients’ survival time.

The gamma-glutamyltraspeptidase (GGT)-to-PLT ratio (GPR) is a newly reported model for evaluating the grade of hepatic fibrosis, which is of great value in predicting hepatic fibrosis\[3-11\]. In June 2015, Lemoine \et al\[3\] first reported that the GPR could be widely used as an independent predictor to assess hepatic fibrosis in CHB patients in West Africa, and that the sensitivity of the GPR is higher than that of the APRI and FIB-4. In November 2015, Boyd \et al\[9\] showed that in patients with HBV and HIV superinfection in France, the GPR can predict the level of significant hepatic fibrosis. In November 2016, Li \et al\[11\] reported that GPR was better than other noninvasive serum models in assessing hepatic fibrosis in CHB patients with high HBV DNA ($\geq 5 \log_{10}$ copies/mL) and normal or mildly elevated alanine transaminase (ALT) ($\leq$ 2 times upper limit of normal (ULN)) in a Chinese population. Moreover, Lemoine \et al\[11\] and Park \et al\[5\] each reported that the GPR could be used as an independent factor in the preoperative evaluation of patients with primary liver cancer caused by CHB. However, likely due to the small sample size, they did not carry out an in-depth stratified pathological study of hepatic fibrosis. Based on these findings, to further explore the value of the GPR in the diagnosis of hepatic fibrosis, we retrospectively analysed a total of 652 outpatients and inpatients diagnosed with CHB at the General Hospital of Ningxia Medical University from May 2010 to January 2016, among whom 390 newly diagnosed CHB patients with complete data without previous...
therapy were examined by correlation analysis and receiver operating characteristic curve (ROC) analysis. The correlations among patient's general information, medical history, and laboratory examination results were determined.

**MATERIALS AND METHODS**

**Case selection**
There were 652 outpatients and inpatients diagnosed with CHB at the General Hospital of Ningxia Medical University from May 2010 to January 2017. Patients with severe heart, brain or kidney disease; severe infection; super infection with hepatitis A virus, hepatitis C virus, hepatitis D virus, or hepatitis E virus or autoimmune liver disease; heavy drinking; or pregnancy were excluded. The remaining 390 newly diagnosed CHB patients, who did not undergo hepatoprotective, anti-hepatic fibrosis drug or antiviral drug treatments, were selected for the study, which included 283 males and 107 females. All CHB patients in the study had a complete medical history; data on HBV serum markers, serum HBV DNA, and liver function; and liver biopsy results. According to the clinical diagnostic criteria in the Guidelines for prevention and treatment of chronic hepatitis B published in 2001, all of the CHB patients were classified and analysed based on liver function and liver fibrosis.

**Clinical indexes**
The clinical characteristics of the CHB patients in this study, including their medical history, HBV serum markers, liver function, blood platelets, serum GGT, hepatic fibrosis indexes (APRI, FIB-4, and GPR), and pathological grade of hepatic fibrosis, were statistically analysed.

**HBV serum marker detection:** Chemiluminescence detection was used to assess HBV serum markers. The equipment and reagents were provided by Abbott Company (United States).

**Liver function and GGT detection:** A kinetic method was used to assess liver function and GGT. An ACX9 automatic biochemical analyser (Beckman Company, United States) was employed for this purpose. The biochemical test kit was also from Beckman. GGT normal range was 10-60 U/L.

**Platelet detection:** An automatic blood cell analyser was used for platelet detection. The normal range was 100-300 × 10^9/L.

**APRI and FIB-4 calculation formulas:** The formulas for calculating the APRI and FIB-4 indexes were as follows: APRI = (AST/ULN) × 100/PLT count (10^9/L) and FIB-4 = (age × AST)/(PLT count × ALT square root). Total bilirubin (TBIL) normal range was 3.4-17.1 μmol/L. AST normal range was 15-40 U/L. ALT normal range was 9-50 U/L.

**Hepatic tissue pathological fibrosis analysis:** The degree of fibrosis was graded from F1 to F4 according to the guidelines on CHB published in 2015.

**Statistical method:** A database of all data was established in Excel2000. The data, expressed as the mean ± SD, were statistically analysed using SPSS17.0 software. Normally distributed data were compared by t-test, and non-normally distributed data were compared using the χ^2 test. In addition, correlations were determined by Pearson correlation analysis. P < 0.05 indicated that the difference was statistically significant. ROC curves were plotted for the GPR, APRI and FIB-4; and the areas under the curve (AUCs) were calculated to determine the optimal cut-off points on the ROC curves corresponding to the greatest sum of the sensitivity and specificity and to calculate the rate of diagnostic accuracy. ROC curve is a graphical plot that illustrates the diagnostic ability of a binary classifier system as its discrimination threshold varies. The ROC curve is created by plotting the true positive rate (TPR) against the false positive rate (FPR) at various threshold settings. The TPR is also known as sensitivity, recall or probability of detection in machine learning. The FPR is also known as the fall-out or probability of false alarm and can be calculated as (1 - specificity). The ROC curve is thus the sensitivity as a function of fall-out. In general, if the probability distributions for both detection and false alarm are known, the ROC curve can be generated by plotting the cumulative distribution function of the detection probability on the Y-axis vs the cumulative distribution function of the false-alarm probability on the X-axis. The value of the GPR, APRI, and FIB-4, as well as the combination of the GPR and APRI or the GPR and FIB-4, in the diagnosis of CHB associated liver fibrosis was evaluated according to the test results. A difference was considered statistically significant at P < 0.05.

**RESULTS**

**Correlation analysis of GPR, APRI, and FIB-4 and clinical data**
A total of 390 patients with CHB were enrolled in this study, including 283 males and 107 females, with a mean age of 38.94 ± 11.39 years. Pearson correlation analysis showed that the GPR, APRI and FIB-4 were not associated with the CHB patients’ age, gender, or the disease course, but were associated with TBil, AST, ALT, GGT, and PLT count (P < 0.01; Table 1).

**Correlation analysis of GPR, APRI, and FIB-4 and CHB liver function classification**
To investigate the relationships between the GPR, APRI
and FIB-4 and CHB disease, the CHB patients were divided into three groups according to their condition: 244 mild cases, 57 moderate cases, and 80 severe cases. Spearman correlation analysis showed that the GPR, APRI, and FIB-4 were positively related to the grade of the CHB patients’ liver function ($P < 0.01$; Table 2).

**Correlation analysis of GPR, APRI, and FIB-4 and hepatic fibrosis stages of CHB**

According to the liver biopsy results, the degrees of hepatic fibrosis was divided into F1 to F4, and the Spearman rank correlation analysis showed that the GPR, APRI, and FIB-4 were positively correlated with the stage of hepatic fibrosis ($P < 0.01$; Table 3).

**ROC analysis of GPR, APRI, and FIB-4 in diagnosis of hepatic fibrosis in CHB**

The AUC values for the GPR in F1, F2, F3, and F4 were 0.723, 0.741, 0.826, and 0.833, respectively, which were significantly higher than the values for the FIB-4 and APRI (F1: 0.581 and 0.612; F2: 0.706 and 0.711; F3: 0.73 and 0.751; and F4: 0.799 and 0.778). The diagnostic cut-off points for each stage were, respectively, 0.402, 0.448, 0.548, and 0.833. The diagnostic sensitivity and specificity had a gradually increasing trend with the aggravation of hepatic fibrosis. In particular, the diagnostic sensitivity and specificity were, respectively, 88.8% and 87.5% in F1, 72.7% and 89.7% in F2, 81.3% and 98.6% in F3, and 80% and 97.4% when GPR and APRI were connected in parallel; 86.6% and 90.2%, 78.4% and 97.4%, and 73.2% and 97.9%, respectively, when GPR and APRI were connected in series; 80.2% and 89%, 65% and 89%, 70.3% and 98.5%, and 78.8% and 96.8%, respectively, when GPR and APRI were connected in parallel; and 83.6% and 87.9%, 76.8% and 96.6%, 72.7% and 98%, and 74.4% and 97.7%, respectively, when GPR and APRI were connected in series (Figure 1, Table 4).

**DISCUSSION**

CHB is an inevitable stage for patients with HBV...
Table 1  Correlation of the GPR, APRI, and FIB-4 (mean ± SD) with the baseline characteristics of patients

| Parameter | Mean ± SD | GPR  | APRI | FIB-4 | P   |
|-----------|-----------|------|------|-------|-----|
| TBIL (μmol/L) | 22.70 ± 28.53 | 0.275 | 0.205 | 0.258 | < 0.01 |
| AST (IU/L) | 81.71 ± 146.11 | 0.183 | 0.644 | 0.834 | < 0.01 |
| ALT (IU/L) | 125.71 ± 246.43 | 0.113 | 0.547 | 0.764 | < 0.01 |
| GGT (IU/L) | 225.21 ± 1088.88 | 0.779 | 0.222 | 0.235 | < 0.01 |
| PLT count (10^3/L) | 160.82 ± 66.61 | -0.285 | -0.285 | -0.26 | < 0.01 |
| GPR | 0.73 ± 1.79 | 1.000 | 0.385 | 0.255 | < 0.01 |
| APRI | 65.44 ± 140.77 | 0.385 | 1.000 | 0.847 | < 0.01 |
| FIB-4 | 417.93 ± 1387.85 | 0.255 | 0.847 | 1.000 | < 0.01 |

TBIL: Total bilirubin; AST: Aspartate transaminase; ALT: Alanine transaminase; GGT: Gamma-glutamyltranspeptidase; PLT: Platelet; GPR: the gamma-glutamyltranspeptidase-to-platelet ratio; APRI: (AST)-to-platelet ratio index; FIB-4: Fibrosis-4.

Table 2  Correlation of the GPR, APRI, and FIB-4 (mean ± SD) with the liver function severity classification

| Parameter | n | GPR  | APRI | FIB-4 |
|-----------|---|------|------|-------|
| Liver function grade mild | 244 | 0.50 ± 0.92 | 30.71 ± 76.73 | 68.39 ± 126.12 |
| r | 0.213 | 0.091 | 0.219 |
| P | < 0.01 | < 0.01 | < 0.01 |
| Moderate | 57 | 1.57 ± 3.39 | 101.20 ± 202.09 | 511.23 ± 1234.61 |
| r | 0.11 | 0.16 | 0.191 |
| P | < 0.01 | < 0.01 | < 0.01 |
| Severe | 80 | 0.84 ± 1.74 | 145.90 ± 192.51 | 1417.54 ± 2544.58 |
| r | 0.036 | 0.563 | 0.720 |
| P | < 0.01 | < 0.01 | < 0.01 |

Table 3  Correlation of the GPR, APRI, and FIB-4 (mean ± SD) with the liver tissue pathological grade

| Fibrosis grade | n | GPR  | APRI | FIB-4 |
|---------------|---|------|------|-------|
| F1 | 122 | 0.54 ± 1.23 | 53.18 ± 134.37 | 331.04 ± 1152.78 |
| r | 0.077 | 0.089 | 0.077 |
| P | < 0.01 | < 0.01 | < 0.01 |
| F2 | 52 | 0.66 ± 2.02 | 47.55 ± 120.04 | 278.98 ± 1053.17 |
| r | 0.223 | 0.069 | 0.037 |
| P | < 0.01 | < 0.01 | < 0.01 |
| F3 | 61 | 0.60 ± 0.95 | 61.15 ± 152.26 | 406.94 ± 1580.52 |
| r | 0.276 | 0.226 | 0.183 |
| P | < 0.01 | < 0.01 | < 0.01 |
| F4 | 41 | 0.52 ± 0.85 | 49.43 ± 125.04 | 287.50 ± 1092.13 |
| r | 0.186 | 0.121 | 0.064 |
| P | < 0.01 | < 0.01 | < 0.01 |

liver biopsy can cause serious complications\cite{14-18}, thus, it is not preferred by most CHB patients in the clinic. Given this situation, strategies for avoiding and reducing the frequency of liver biopsy and obtaining reliable liver pathological data are urgently needed\cite{19-21}. The APRI and FIB-4 were developed as serum models in recent years and have been widely used in the assessment of hepatic fibrosis classification\cite{22-26}. However, for patients with severe liver inflammation, the hepatic fibrosis results yielded by the APRI and FIB-4 are variable. Therefore, these indexes are predominantly used for hepatic fibrosis evaluation in patients with mildly abnormal liver function before treatment. Recently, Lemoine et al\cite{3} analysed the combination of GGT and PLT count and found that the GPR was significantly better than the FIB-4 and APRI in predicting significant liver fibrosis. However, due to the sample size, the depth of the study was limited. To further explore the value of applying the GPR, a correlation analysis of 390 newly diagnosed CHB patients who were not treated with hepatoprotective therapy, anti-liver fibrosis drugs, or antiviral drugs to assess the correlation of the GPR, APRI, and FIB-4 with age, gender, medical history, liver function (TBil, ALT, AST), GGT, PLT count, and liver tissue fibrosis stage. The results showed that the GPR, APRI, and FIB-4 did not have a correlation with the CHB patients’ age, gender, or duration, but were correlated with TBil, AST, ALT, GGT, PLT count, and liver tissue fibrosis stage. The results showed that the GPR, APRI, and FIB-4 were positively associated with liver function and liver tissue pathological grade (P < 0.01). These results indicate that the GPR, as well as the APRI and FIB-4, can not only be used as an index to judge the severity of acute liver injury, but also has potential value in evaluating the degree of hepatic fibrosis in patients with CHB.

To further analyse the value of the GPR for the diagnosis of hepatic fibrosis, we performed ROC analysis of the GPR, APRI, and FIB-4 according to the stage of liver fibrosis. The results showed that the AUC values for GPR in F1, F2, F3, and F4 were 0.723, 0.741, 0.826 and 0.833, respectively, which were significantly better than the values for the APRI and FIB-4 (F1: 0.581 and 0.612; F2: 0.706 and 0.711; F3: 0.73 and
ARTICLE HIGHLIGHTS

Research background
Hepatic fibrosis is a precursor of cirrhosis in patients with chronic hepatitis B (CHB). Severe hepatic fibrosis and cirrhosis can increase the incidence and mortality of primary liver cancer. Looking for a non-invasive, simple, easy to operate, cheap way to assess liver fibrosis is very important.

Liver biopsy is still the gold standard for the diagnosis of liver fibrosis, but it is not widely used as a routine examination because of its invasiveness, high cost, and lack of repeatability. As an alternative, transient elastography (Fibroscan) by imaging is considered a good tool for the diagnosis of hepatic fibrosis, but its performance is restricted by several factors. As an alternative, transient elastography (Fibroscan) by imaging is considered a good tool for the diagnosis of hepatic fibrosis, but its performance is restricted by several factors.

Researchers have tried to identify a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level, which could assist in early diagnosis to achieve timely treatment, delay cirrhosis or liver cancer occurrence, improve patients’ quality of life, and prolong patients’ survival time.

Research motivation
At present, liver biopsy is still the gold standard for the diagnosis of liver fibrosis, but liver biopsy can cause serious complications; thus, it is not preferred by most CHB patients in the clinic. Our study aimed to identify a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level.

Research objectives
Our study aimed to identify a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level. In the future, in our clinical work, assessing the level of liver fibrosis in patients is faster and easier, effectively avoiding the complications caused by liver biopsy.

Research methods
There were 652 outpatients and inpatients diagnosed with CHB at the General Hospital of Ningxia Medical University. Patients with severe heart, brain or kidney disease; severe infection; superinfection with hepatitis A virus, hepatitis C virus, hepatitis D virus, or hepatitis E virus or autoimmune liver disease; heavy drinking; or pregnancy were excluded. The remaining 390 newly diagnosed CHB patients, who did not undergo hepatoprotective, anti-hepatic fibrosis drug, or antiviral drug treatments, were selected for the study. We chose multiple noninvasive indicators for comparison, to illustrate that GPR is an optimal noninvasive index. Meanwhile, the sample size was large to enhance persuasiveness. Statistically analysed using SPSS17.0 software, the data are expressed as the mean ± SD. Normal distributed data were compared using the Chi-square test. In addition, correlations were determined by Pearson correlation analysis; P < 0.05 indicated that the difference was statistically significant.

Research results
The GPR is a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level, and it can significantly improve the sensitivity and specificity of hepatic fibrosis diagnosis in CHB when combined with the FIB-4 or APRI.

Research conclusions
The GPR is a newly reported model for evaluating the grade of hepatic fibrosis, which is of great value in predicting hepatic fibrosis. In June 2015, Lemoine et al first reported that the GPR could be widely used as an independent predictor to

Table 4  GPR, APRI, and FIB-4 results relative to hepatic fibrosis stage (F1, F2, F3, and F4) in CHB patients

| Parameter | GPR | APRI | FIB-4 | GPR + APRI (in parallel) | GPR + APRI (in series) | GPR + FIB-4 (in parallel) | GPR + FIB-4 (in series) |
|----------|-----|------|------|-------------------------|------------------------|--------------------------|------------------------|
| AUC      | 0.723 | 0.581 | 0.612 | -                        | -                      | -                        | -                      |
| Cut-off  | 0.448 | 0.166 | 0.201 | -                        | -                      | -                        | -                      |
| F1 Sensitivity | 90.6% | 88.8% | 62.1% | 92.9%                   | 88.5%                  | 90.2%                    | 89%                    |
| Specificity | 54.2% | 87.5% | 66.3% | 78.7%                   | 89%                    | 87%                      | 85%                    |
| AUC      | 0.741 | 0.706 | 0.711 | -                        | -                      | -                        | -                      |
| Cut-off  | 0.402 | 0.361 | 0.4    | -                        | -                      | -                        | -                      |
| F2 Sensitivity | 57.1% | 75.8% | 47.4% | 71.7%                   | 65%                    | 76.8%                    | 72.7%                  |
| Specificity | 89.5% | 92.5% | 89.3% | 92.7%                   | 96.6%                  | 97.8%                    | 98%                    |
| AUC      | 0.826 | 0.73  | 0.751 | -                        | -                      | -                        | -                      |
| Cut-off  | 0.548 | 0.496 | 0.44  | -                        | -                      | -                        | -                      |
| F3 Sensitivity | 74.1% | 70.6% | 64.7% | 81.3%                   | 70.3%                  | 72.7%                    | 72.7%                  |
| Specificity | 91.8% | 90.5% | 88%   | 98.6%                   | 98%                    | 98%                      | 98%                    |
| AUC      | 0.833 | 0.799 | 0.778 | -                        | -                      | -                        | -                      |
| Cut-off  | 0.591 | 0.538 | 0.503 | -                        | -                      | -                        | -                      |
| F4 Sensitivity | 83.2% | 74%   | 75.4% | 80%                     | 74.4%                  | 74.4%                    | 74.4%                  |
| Specificity | 96.5% | 95.4% | 94.5% | 97.4%                   | 97%                    | 97%                      | 97%                    |

In parallel: Both parameters are met simultaneously; In series: One of two parameters is met.
assess hepatic fibrosis in CHB patients in West Africa, and that the sensitivity of the GPR is higher than those of the APRI and FIB-4. GPR is a simple, convenient, cheap, and noninvasive index to assess patients’ hepatic fibrosis level, and it can significantly improve the sensitivity and specificity of hepatic fibrosis diagnosis in CHB when combined with the FIB-4 or APRI. In the future, in our clinical work, assessing the level of liver fibrosis in patients is faster and easier, effectively avoiding the complications caused by liver biopsy.

Research perspectives
In the future work, it is required to look for more noninvasive, convenient and efficient methods to assess the level of liver fibrosis in patients with chronic hepatitis B.

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