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ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Cesare Tosetti, MD, Doctor, Professor, Department of Primary Care, Health Care Agency of Bologna, Porretta Terme 40046, Bologna, Italy

AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 642 experts in gastroenterology and hepatology from 59 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

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World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central and Directory of Open Access Journals. The 2018 edition of Journal Citation Reports® cites the 2017 impact factor for *WJG* as 3.300 (5-year impact factor: 3.387), ranking *WJG* as 35th among 80 journals in gastroenterology and hepatology (quartile in category Q2).

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Ze-Mao Gong, Director
World Journal of Gastroenterology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: http://www.f6publishing.com/helpdesk
http://www.wjgnet.com

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpgoffice@wjgnet.com
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ORIGINAL ARTICLE

Case Control Study

Evaluation of elastography combined with serological indexes for hepatic fibrosis in patients with chronic hepatitis B

Bin Xu, Ning-Ming Zhou, Wei-Tian Cao, Xiao-Jing Li

Bin Xu, Ning-Ming Zhou, Wei-Tian Cao, Department of ultrasound, Fudan University affiliated Shanghai fifth people's hospital, Shanghai 200240, China

Xiao-Jing Li, Department of pathology, Fudan University affiliated Shanghai fifth people's hospital, Shanghai 200240, China

ORCID number: Bin Xu (0000-0002-9184-107X); Ning-Ming Zhou (0000-0001-8424-7825); Wei-Tian Cao (0000-0002-4880-7589); Xiao-Jing Li (0000-0001-6370-9146).

Author contributions: Xu B designed research; Xu B, Cao WT, Li XJ performed research; Zhou NM contributed new reagents or analytic tools; Li XJ analyzed data; Xu B wrote the paper.

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Correspondence to: Ning-Ming Zhou, MD, Chief Doctor, Department of ultrasound, Fudan University affiliated Shanghai fifth people's hospital, 128 Ruili road, Minhang district, Shanghai 200240, China. zhouningming@5thhospital.com
Telephone: +86-21-24289356
Fax: +86-21-24289356

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Abstract

AIM

To investigate the value of ultrasound elastography combined with serological indexes in diagnosing liver fibrosis and assessing its severity.

METHODS

A total of 338 chronic hepatitis B (CHB) patients were divided into a disease group (patients with hepatic fibrosis) and control group (subjects without hepatic fibrosis). The disease group was further divided into S1-S4 according to the degree of fibrosis. Independent risk factors for hepatic fibrosis were analyzed using multivariate logistic regression. The diagnostic values of hepatic fibrosis from different indicators were compared using receiver operating characteristic (ROC) curves. The combination of elastography and serological indexes was explored to assess the severity of hepatic fibrosis.

RESULTS

The multivariate logistic regression analysis results revealed that shear wave velocity (SWV), hyaluronic acid (HA), type Ⅳ collagen (CⅣ) and aspartate aminotransferase-to-platelet ratio index (APRI) significantly affected the occurrence of hepatic fibrosis. The ROC curve revealed that the accuracy of the diagnosis of hepatic fibrosis for SWV and HA were 87.3% and 84.8%, respectively. The accuracy of SWV combined with HA was 88.9%. The multiple linear regression analysis revealed that SWV, aspartate aminotransferase (AST)/alanine aminotransferase (ALT), HA, CⅣ, APRI and fibrosis index based on the 4 factor (FIB-4) were screened as statistically significant independent factors. The established regression equation was: Fibrosis level = -4.046 + 1.024 × SWV + 1.170 × AST/ALT + 0.011 × HA + 0.020 × CⅣ + 0.719 × APRI + 0.379 × FIB-4.

CONCLUSION

SWV combined with serological indexes can improve the accuracy of diagnosis for CHB hepatic fibrosis. Serum indexes can help diagnose the degree of hepatic fibrosis.

Key words: Elastography; Serology; Hepatic fibrosis; Non-invasive diagnosis

Core tip: Hepatic fibrosis affects the physiological function of the liver. The current assessment method for the degree of hepatic fibrosis is still unreliable. This study found that the shear wave velocity of ultrasound elastography can improve the accuracy of the diagnosis of hepatic fibrosis. Its combination with serological indicators (aspartate aminotransferase/alanine aminotransferase, hyaluronic acid, type Ⅳ collagen, aspartate aminotransferase-to-platelet ratio index and fibrosis index based on the 4 factor) can further help in the clinical assessment of the degree of hepatic fibrosis.

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INTRODUCTION

Hepatic fibrosis is a pathological change caused by chronic liver injury, which in turn affects the physiological function of the liver[1-4]. Pathological examination is the gold standard for the diagnosis of hepatic fibrosis, which enables a definitive diagnosis of hepatic fibrosis[5-8]. However, pathological examination mainly relies on biopsy. Biopsy is a kind of invasive examination with the drawbacks of poor reproducibility and sampling errors. Therefore, non-invasive diagnostic methods that seek repeatable measurements have presently become research hotspots. At present, serological indexes are the main clinical methods to assess hepatic fibrosis, although the accuracy needs to be improved[9-11]. The latest research has shown that ultrasound elastography can measure the hardness of liver tissue to determine the degree of hepatic fibrosis with features of non-invasiveness, simplicity, speed and repeatability[12,13]. However, its diagnostic accuracy is not high, and the accuracy of different studies are different[14,15]. Hence, we still need to explore the diagnostic methods of hepatic fibrosis, as well as search for a reliable method to assess the degree of hepatic fibrosis. The investigators therefore collected patients who were admitted to our hospital with chronic hepatitis B (CHB) as subjects in the present study. Their final pathological results were used as a basis for the diagnosis of hepatic fibrosis, and the serological indexes and ultrasound elastography data of these patients were analyzed. The aim of the present study was to search for an optimal method for the combined diagnosis of hepatic fibrosis, and establish an optimal non-invasive assessment model for the severity of hepatic fibrosis.

MATERIALS AND METHODS

Research object

A total of 338 CHB patients were randomly enrolled in our hospital from January 2015 to June 2017. Among these patients, 200 patients were male and 138 patients were female. Inclusion criteria: (1) Patients who underwent liver biopsy; and (2) patients who received ultrasound elastography and serological detection before the biopsy. Exclusion criteria: (1) Patients combined with other types of liver disease; (2) patients with severe heart, liver and kidney insufficiency, coma, or puncture site infection; and (3) patients associated with liver cancer, immune system disease, or active bleeding and other diseases. These patients were divided into two groups according to the presence of hepatic fibrosis *via* biopsy: disease group (patients with hepatic fibrosis) and control group (subjects without hepatic fibrosis). The disease group was further divided into four subgroups, according to the degree of fibrosis: S1, S2, S3 and S4. All patients or their families provided a signed informed consent. The present study met the requirements of the hospital ethics committee and received their approval.

Research methods

Detection of hepatitis B hepatic fibrosis *via* acoustic radiation force impulse: The acoustic radiation force impulse (ARFI) test was performed using an ACOUSON S2000 Color Ultrasound Scanner (Siemens). (1) The patient underwent fasting and was placed in the left lateral decubitus position, with the right-hand on the head. Then, the right hepatic tissue of the liver was detected; (2) the elastic sampling frame was placed perpendicular to the

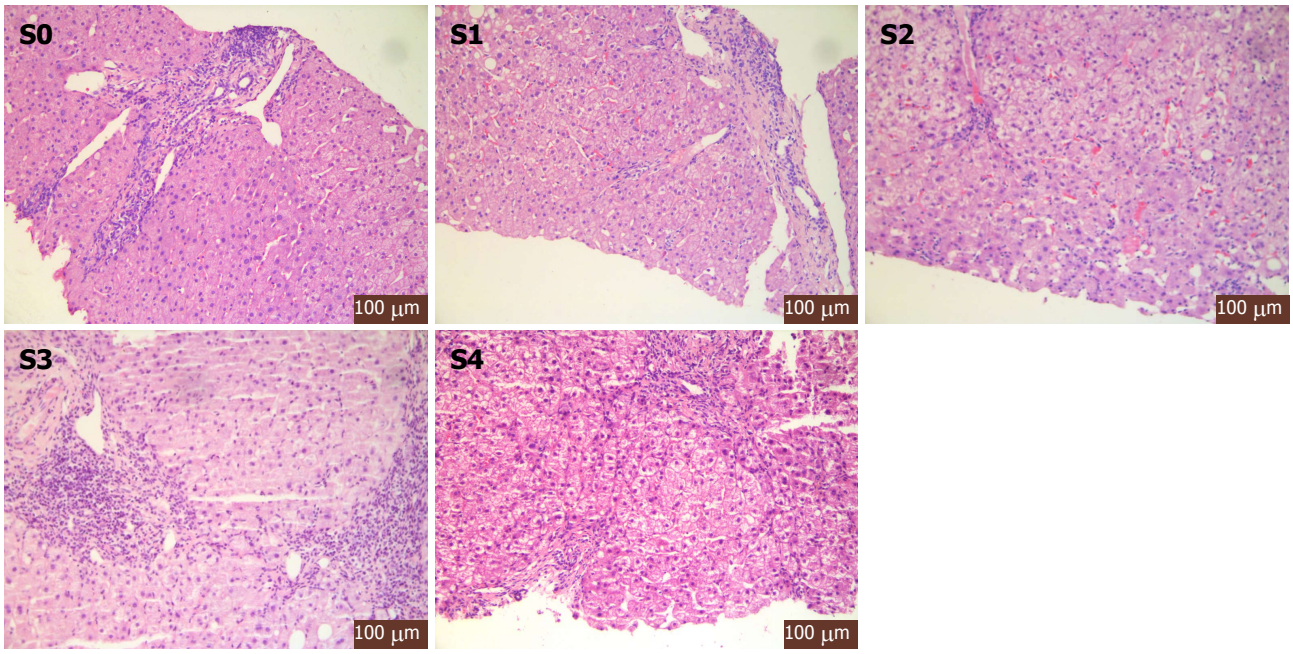

Figure 1 Histopathology of different pathological stages of hepatic fibrosis. S0 phase: No fibrosis; S1 phase: Fibrous enlargement in the portal area, but no fibrillary septum formation; S2 phase: Fibrosis enlargement in the portal area, a few fibrous septae formed; S3 stage: Most fibrous septae formed but no hardened nodules; S4 stage: Liver cirrhosis.

liver surface, and then placed in the liver parenchyma at approximately 4 cm away from the probe surface in order to avoid the surrounding blood vessels. The patient was instructed to hold their breath; and (3) the update key was pressed, a high-intensity low-frequency pulse wave was launched, the transverse shear wave velocity (SWV) was received in m/s, and the value was recorded. The measurement was repeated three times, and the SWV value was taken as the SWV value of the liver parenchyma.

Serological examination: On the next day of admission, 3 mL of fasting venous blood was collected in the morning. Alanine aminotransferase (ALT), aspartate transaminase (AST), blood platelet (PLT), total bilirubin (TBIL), hyaluronic acid (HA) levels, laminin (LN), type Ⅳ collagen (CⅣ), and type Ⅲ procollagen (PⅢNP) were measured. Serum ALT, AST, PLT and TBIL were detected using an automatic biochemical analyzer, while HA, LN, CⅣ and PⅢNP were measured by photochemiluminescence. APRI score: the AST and platelet (PLT) ratio index (aspartate aminotransferase-to-platelet ratio index, APRI). APRI = [(AST/ULN) × 100/PLT (10^9/L)][16]. FIB-4 index: FIB-4 = (age × AST) ÷ (platelet ×√ALT).

Liver biopsy: Liver tissue biopsies were simultaneously performed with ultrasound elastography and serological tests. The subjects were placed in the supine position, the preoperative ultrasound was localized, and the liver puncture was performed under ultrasound guidance. The puncture gun was an automatic biopsy gun obtained from Bard Inc. (United States), with a 16 G disposable biopsy. The needle biopsy was performed in the ARFI sampling frame area. Liver biopsy was conducted with routine disinfection, which was covered with a towel, and local anesthesia with 5% lidocaine was given to avoid the visible pipeline in the liver. A tissue length of 1-2 cm was removed. The degree of hepatic fibrosis in patients with CHB was determined based on histological staging criteria, according to the "Guidelines for the Prevention and Treatment of Chronic Hepatitis B (2015 Update version)". In particular, S0 phase refers to patients with no fibrosis, the S1 phase refers to patients with enlarged fibrosis in the portal area but no fibril septum formation, the S2 phase refers to patient with a fibrous enlargement in the portal area and minimal fibrillary septae formation, the S3 phase refers to patients with the most fibrillary septae formed but without hardened nodules, and the S4 phase refers to patients with cirrhosis (Figure 1).

Statistical analysis

Statistical analysis was performed using SPSS 19.0 and MedCalc software. Measurement data were expressed as mean ± SD. The *t*-test was used for comparisons between the two groups. The rate of adoption of count data was expressed using a Chi-square test to compare the two groups. Independent risk factors of fibrotic liver were analyzed by multivariate logistic regression analysis, while ROC curve analysis was conducted to determine the accuracy in the diagnosis of hepatic fibrosis. Spearman correlation analysis was used to compare the degree of hepatic fibrosis with serological markers and elastography. Multiple linear regression was used to establish a hepatic fibrosis assessment model and determine its degree of fit. $P < 0.05$ was considered

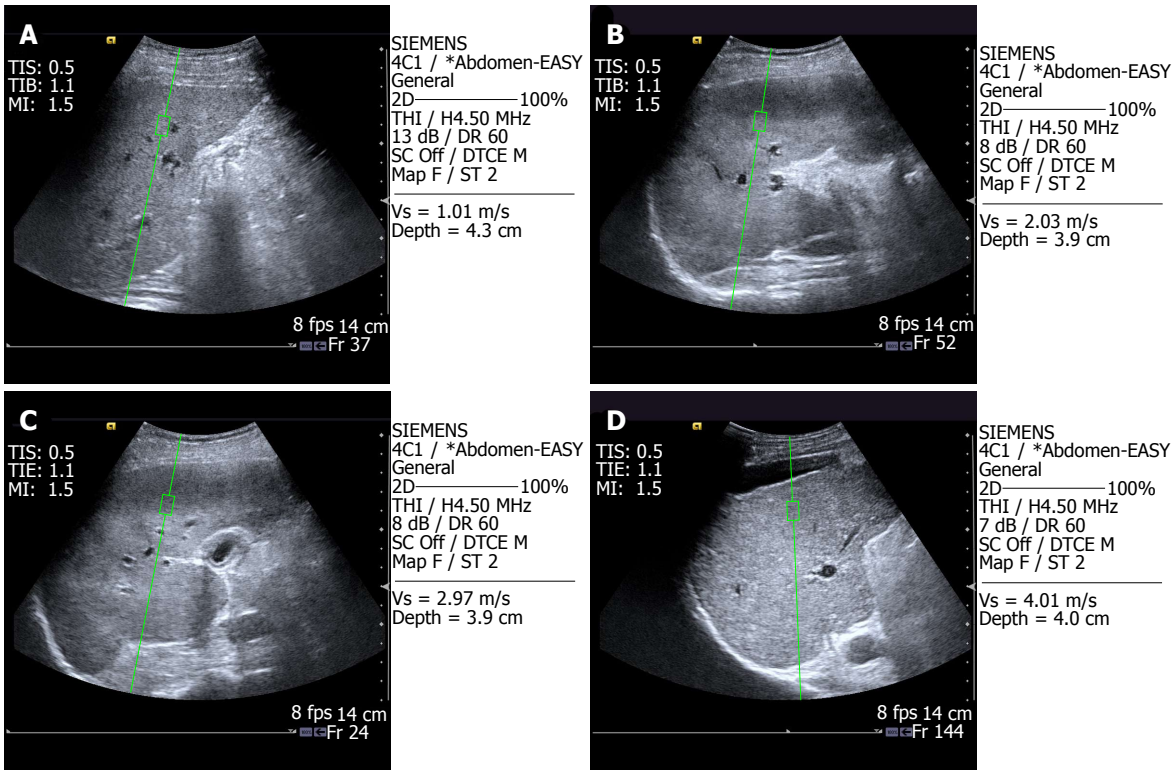

Figure 2 Image of hepatic fibrosis assessed by acoustic radiation force impulse to assess liver tissue elasticity. A: Normal liver tissue, SWV = 1.01 m/s; B: Mild hepatic fibrosis, SWV = 2.03 m/s; C: Moderate hepatic fibrosis, SWV = 2.97 m/s; D: Severe hepatic fibrosis, SWV = 4.01m/s. ARFI: Acoustic radiation force impulse.

Table 1 Comparison of clinical data in the two groups

	Hepatic fibrosis group (n = 245)	Control group (n = 93)	t/χ^2 value	P value
Sex (male/%)	136/55.51	45/48.39	1.375	0.241
Age	40.31 ± 10.47	37.82 ± 13.72	1.785	0.075
SWV (m/s)	3.02 ± 0.80	1.52 ± 0.62	16.310	0.000
ALT (U/L)	52.23 ± 26.02	46.87 ± 87.45	1.487	0.138
AST (U/L)	41.12 ± 12.72	36.14 ± 14.52	1.607	0.109
AST/ALT	0.93 ± 0.41	0.74 ± 0.23	4.221	0.000
PLT (10^9/L)	184.02 ± 02.21	192.37 ± 37.42	1.220	0.223
TBIL (μmol/L)	19.83 ± 9.83	18.75 ± 8.72	1.570	0.117
HA (μg/L)	113.24 ± 24.78	63.23 ± 23.54	15.748	0.000
LN (μg/L)	36.21 ± 21.34	34.21 ± 10.28	1.485	0.139
CⅣ (μg/L)	33.28 ± 28.20	20.89 ± 9.56	4.144	0.000
PⅢNP (μg/L)	36.29 ± 29.45	32.87 ± 2.32	1.100	0.272
APRI	0.85 ± 0.61	0.62 ± 0.52	3.219	0.001
FIB-4	1.63 ± 0.89	1.17 ± 0.62	4.578	0.000

SWV: Shear wave velocity; ALT: Alanine aminotransferase; AST: Aspartate transaminase; PLT: Blood platelet; TBIL: Total bilirubin; HA: Hyaluronic acid; LN: Laminin; CⅣ: Type Ⅳ collagen; PⅢNP: Type Ⅲ procollagen; APRI: Aspartate aminotransferase-to-platelet ratio index; FIB-4: Fibrosis index based on the 4 factor.

statistically significant.

RESULTS

Comparison of clinical data

A total of 338 patients were enrolled in the present study. Among these patients, 93 subjects were assigned to the control group, while 245 patients were assigned to the disease group. Among the patients in the disease group, 72 patients were in the S1 phase, 65 patients were in the S2 phase, 58 patients were in the S3 phase, and 50 patients were in the S4 phase. Furthermore, among the 245 patients in the disease group, 62 patients had mild hepatic fibrosis, 176 patients had moderate hepatic fibrosis, and seven patients had severe hepatic fibrosis (Figure 2). The serological indexes, such as AST/ALT, HA, CⅣ, APRI and FIB-4, were significantly greater in the disease group than in the control group, and the differences were statistically significant (P < 0.05). For the elastography, SWV was significantly greater in the disease group than in the control group, and the difference was statistically significant (P < 0.05). The remaining indicators were similar between the two groups, and the difference was not statistically significant (P > 0.05) (Table 1).

Multivariate analysis of hepatic fibrosis

Indicators with significant differences (SWV, AST/ALT, HA, CⅣ, APRI and FIB-4) were used as independent variables. The occurrence of fibrosis was a dependent variable, and a multivariate logistic regression analysis was conducted. These results revealed that SWV, HA, CⅣ and APRI had a significant effect on hepatic fibrosis (P < 0.05). According to the OR value, the sequence was SWV, HA, APRI and CⅣ (Table 2).

Diagnosis of different indicators in hepatic fibrosis

The ROC curve for the diagnosis of hepatic fibrosis by

Table 2 Binary logistic regression analysis of risk factors associated with hepatic fibrosis

Influencing factors	B	SE	Wald	OR	95%CI	*P* value
SWV	0.931	0.325	5.024	2.537	1.342-4.797	0.025
AST/ALT	0.561	0.286	2.765	1.752	0.896-3.069	0.056
HA	0.838	0.127	5.352	2.311	1.802-2.964	0.021
CⅣ	0.466	0.183	4.042	1.593	1.113-2.280	0.046
APRI	0.719	0.312	4.642	2.053	1.114-3.784	0.037
FIB-4	0.433	0.287	2.973	1.542	0.879-2.706	0.063

SWV: Shear wave velocity; ALT: Alanine aminotransferase; AST: Aspartate transaminase; HA: Hyaluronic acid; CⅣ: Type Ⅳ collagen; APRI: Aspartate aminotransferase-to-platelet ratio index; FIB-4: Fibrosis index based on the 4 factor.

Table 3 Diagnostic efficacy of various indicators in the diagnosis of hepatic fibrosis

Index	AUC	Best diagnostic point	Sensitivity, %	Specificity, %
SWV	0.873	1.66 m/s	86.90	88.20
AST/ALT	0.803	0.920	55.90	95.70
HA	0.848	87.79 μg/L	91.00	79.60
CⅣ	0.784	30.36 μg/L	52.70	98.90
APRI	0.789	0.787	57.60	86.00
FIB-4	0.797	1.157	80.00	65.60

SWV: Shear wave velocity; ALT: Alanine aminotransferase; AST: Aspartate transaminase; HA: Hyaluronic acid; CⅣ: Type Ⅳ collagen; APRI: Aspartate aminotransferase-to-platelet ratio index; FIB-4: Fibrosis index based on the 4 factor.

Table 4 Correlation between serological data and the degree of hepatic fibrosis

Index	r	*P* value
SWV (m/s)	0.767	0.000
HA (μg/L)	0.711	0.000
AST/ALT	0.684	0.000
CⅣ (μg/L)	0.681	0.000
APRI	0.634	0.000
FIB-4	0.702	0.000

SWV: Shear wave velocity; HA: Hyaluronic acid; ALT: Alanine aminotransferase; AST: Aspartate transaminase; CⅣ: Type Ⅳ collagen; APRI: Aspartate aminotransferase-to-platelet ratio index; FIB-4: Fibrosis index based on the 4 factor.

each index is illustrated in Figure 3. The area under the curve (AUC) for hepatic fibrosis diagnosed by SWV was the highest (0.873), followed by HA (0.848). The remaining AUC rankings were as follows: AST/ALT, APRI, FIB-4, and CⅣ (Figure 3). The combined diagnosis of SWV and HA with the highest AUC indicated that diagnostic accuracy was further improved with an AUC of 0.889 (sensitivity: 95.92% and specificity: 72.04%) (Table 3 and Figure 4).

Association of serological markers with elastography and hepatic fibrosis

Spearman correlation analysis revealed that hepatic fibrosis was positively correlated with SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 levels. The R values were 0.767, 0.684, 0.711, 0.681, 0.634 and 0.702, respectively, and the difference was statistically significant (all $P < 0.05$) (Table 4). The statistically significant indicators in the correlation analysis were included in the multiple linear regression analysis. The results revealed that SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 were selected as statistically significant independent factors, and the constant analysis was statistically significant. The following regression equation was established: degree of fibrosis = -4.046 + 1.024 × SWV + 1.170 × AST/ALT + 0.011 × HA + 0.020 × CⅣ + 0.719 × APRI + 0.379 × FIB-4 (Table 5).

DISCUSSION

CHB is one of the most common causes of liver-related diseases[17-21], which can gradually develop into hepatic fibrosis, cirrhosis and liver cancer[22-30]. At present, hepatic fibrosis remains a reversible process. Its early diagnosis, as well as its timely and effective treatment, can delay or avoid the development of irreversible cirrhosis stages. Developing an approach to simply and correctly evaluate the severity of hepatic fibrosis has become a clinical challenge that needs to be solved[31]. The literature revealed that liver pathology biopsy is the most important diagnostic basis for the diagnosis of hepatic fibrosis[32-34]. Although it is the "gold standard" for the diagnosis of hepatic fibrosis, it requires immense invasiveness and demonstrates poor reproducibility. Imaging and serological examination can reflect hepatic fibrosis. However, neither of them can be used as an independent diagnostic indicator. Elastography has been used to measure shear waves in liver tissues by ultrasound. The speed of ultrasound propagation is used to calculate the hardness of the liver and determine the degree of hepatic fibrosis. Changes in serological indexes reflect the progression of the disease in patients with hepatic fibrosis[35-44]. In this study, in order to search for non-invasive methods for the diagnosis of hepatic fibrosis, 245 patients with hepatic fibrosis and 93 subjects without hepatic fibrosis were used as observation subjects. The general data, elastography and serological indicators of these subjects were used to analyze the feasibility of ultrasound elastography combined with serological markers for the diagnosis of hepatic fibrosis and the degree of hepatic fibrosis.

The present study first analyzed the clinical data of these two groups. The results revealed that SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 were significantly greater in the disease group than in the control group. This suggests that SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 are the six indicators that can help in the clinical screening for patients with hepatic fibrosis, which is consistent with previous studies[45-50]. Subsequently, in the present study, a multivariate logistic regression analysis was performed on these indicators, which showed significant differences. These results revealed that SWV, HA, CⅣ and APRI

Table 5 Multiple linear regression analysis of the degree of hepatic fibrosis

	Non-standardized coefficient		Standard coefficient	*t*	Sig.
	B value	Standard error	*B* value		
Constant	-4.046	0.209	-	-19.365	0.000
SWV	1.024	0.148	0.2200	6.930	0.000
AST/ALT	1.170	0.190	0.3231	7.861	0.000
HA	0.011	0.005	0.2010	7.126	0.000
CⅣ	0.020	0.003	0.1980	5.749	0.000
APRI	0.719	0.102	0.1880	7.040	0.000
FIB-4	0.379	0.088	0.1490	4.304	0.000

SWV: Shear wave velocity; ALT: Alanine aminotransferase; AST: Aspartate transaminase; HA: Hyaluronic acid; CⅣ: Type Ⅳ collagen; APRI: Aspartate amino-transferase-to-platelet ratio index; FIB-4: Fibrosis index based on the 4 factor.

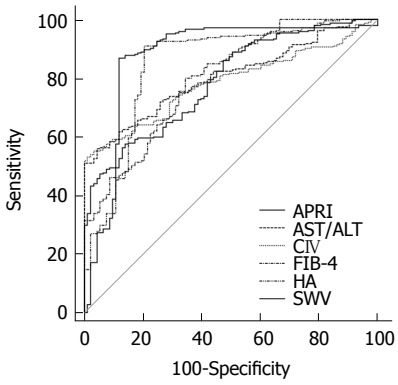

Figure 3 Receiver operating characteristic curve for the diagnosis of hepatic fibrosis based on different indicators. APRI: Aspartate amino-transferase-to-platelet ratio index; AST: Aspartate transaminase; ALT: Alanine aminotransferase; CⅣ: Type Ⅳ collagen; FIB-4: Fibrosis index based on the 4 factor; HA: Hyaluronic acid; SWV: Shear wave velocity.

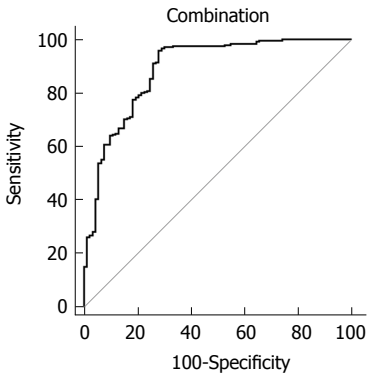

Figure 4 Receiver operating characteristic curve for the diagnosis of hepatic fibrosis based on different combined indicators.

had a significant effect on the development of hepatic fibrosis, suggesting that clinical attention should be given to patients with high levels of SWV, HA, CⅣ and APRI. In order to further explore the clinical significance of these indicators, an ROC curve analysis was performed. Among these four indicators, the maximum area under the ROC curve for SWV was 0.873, suggesting that SWV may be used as an ideal indicator for hepatic fibrosis screening. After these indicators were combined, it was noted that the accuracy of the diagnosis was further enhanced, suggesting that the clinical accuracy of hepatic fibrosis can be improved by combining SWV with serological indexes.

In order to fully explain the effects of SWV and serological indexes on hepatic fibrosis in patients with clinical hepatic fibrosis, correlation analyses and multiple linear regression analyses were performed. The results revealed that the degree of hepatic fibrosis and SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 were positively correlated. After multiple linear regression analysis, the results revealed that SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 were independent factors that affected the degree of hepatic fibrosis, and these were further established. Multiple linear regression equation: Degree of fibrosis = -4.046 + 1.024 × SWV + 1.170 × AST/ALT + 0.011 × HA + 0.020 × CⅣ + 0.719 × APRI + 0.379 × FIB-4. A non-invasive clinical tool was provided for assessing hepatic fibrosis. The SPSS software can be used in clinic to assess the extent of the hepatic fibrosis in a patient by entering the above parameters. Although the richness degree of data collected in the present study can be further improved, the present single-center study was not sufficient to fully guarantee the reliability of the study. Hence, the equation cannot be used as a clinical tool to predict lymph node metastasis. However, this method is worthy of further clinical validation and promotion. In addition, for serological indexes that can reflect the degree of hepatic fibrosis, further review of the literature is needed to explore the mechanism of the degree of fibrosis of the indicator response. This will allow us to obtain a deeper understanding of the significance of serological indexes in the diagnosis of hepatic fibrosis.

In summary, SWV can improve the accuracy of hepatic fibrosis diagnosis, and overcomes the invasive and poor reproducibility shortcomings associated with liver biopsy. At the same time, SWV in combination with serological indexes can further help in the clinical assessment of the extent of hepatic fibrosis in patients.

ARTICLE HIGHLIGHTS

Research background

Pathological examination is known to be the gold standard for diagnosing

liver fibrosis, as it enables a clear diagnosis of liver fibrosis grading. However, pathological examination is an invasive examination and cannot be used as a screening tool. At present, the degree of liver fibrosis is mainly evaluated by serological indicators in the clinic, however the accuracy is relatively low. With advances in technology, ultrasound elastography can be used to assess liver tissue stiffness, although the accuracy is not high. Therefore, it is necessary to explore reliable methods for diagnosing liver fibrosis and assessing the degree of liver fibrosis.

Research motivation

The motivation of this study is to find a more suitable method for the combined diagnosis of liver fibrosis and to establish an optimal non-invasive model for assessing the severity of liver fibrosis. This will provide a reference for non-invasive screening of liver fibrosis.

Research objectives

This study enrolled patients with chronic hepatitis B (CHB) as the research subjects. The aim of this study is to analyze serum markers and ultrasound elastography indicators for diagnosing liver fibrosis and liver fibrosis grading based on pathological results.

Research methods

According to the results of liver biopsy, 338 patients with CHB admitted to our hospital were divided into a diseased group and control group. The diseased group continued to be divided into four groups according to the degree of fibrosis. General data, shear wave velocity (SWV), and serological markers were compared between the two groups. Further independent risk factors for liver fibrosis in patients were analyzed by logistic regression. The accuracy of different indicators in diagnosing liver fibrosis was compared by receiver operating characteristic (ROC) curves. The correlation between different fiber levels and serum indicators or elastography indicators was analyzed. Finally, a multivariate linear regression was used to establish a mathematical model for assessing the severity of liver fibrosis with elastography combined with serological markers.

Research results

SWV, aspartate aminotransferase (AST)/alanine aminotransferase (ALT), hyaluronic acid (HA), type-Ⅳ collagen (CⅣ), aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis index based on the 4 factor (FIB-4) were significantly higher in the disease group than in the control group ($P < 0.05$). The multivariate logistic regression analysis results revealed that SWV, HA, CⅣ and APRI significantly affected the occurrence of hepatic fibrosis. The ROC curve revealed that the accuracy of the diagnosis of hepatic fibrosis for SWV and HA were 87.3% and 84.8%, respectively. The accuracy of SWV combined with HA was 88.9%. Spearman correlation analysis revealed that hepatic fibrosis was positively correlated with SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 levels. The R values were 0.767, 0.684, 0.711, 0.681, 0.634 and 0.702, respectively, and the difference was statistically significant (all $P < 0.05$). The multiple linear regression analysis revealed that SWV, AST/ALT, HA, CⅣ, APRI and FIB-4 were screened as statistically significant independent factors. The established model was: fibrosis level = -4.046 + 1.024 × SWV + 1.170 × AST/ALT + 0.011 × HA + 0.020 × CⅣ + 0.719 × APRI + 0.379 × FIB-4.

Research conclusions

SWV can non-invasively and effectively diagnose liver fibrosis. SWV combined with serological indicators can further improve the accuracy of diagnosing liver fibrosis. The multiple linear regression equation established by SWV combined with serological indicators is expected to be a non-invasive tool for assessing the degree of liver fibrosis.

Research perspectives

This study is a single-center study, and the sample size is limited and insufficient to fully guarantee the reliability of the study. Therefore, the equation we established cannot be used as an accurate tool for clinical prediction of lymph node metastasis, but it is worthy of further clinical validation and promotion. In addition, for serological indicators that can reflect the degree of liver fibrosis, we can further consult the literature to explore the mechanism of the degree of fibrosis. This would help us understand the diagnostic significance of serological markers with respect to the degree of liver fibrosis.

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