

## Mechanisms and Diagnostic Progress of Liver Injury in Hepatitis B Cirrhosis Based on Large Data Analysis

Guo Yan, Chen Jie

Clinical Skills Laboratory Center, Kunming Medical University HaiYuan College, Kunming, 650106, China

**Keywords:** Large Data Technology; Serum Model of Liver Fibrosis; Diagnostic Technology of Liver Cirrhosis and Liver Injury; Screening of Serum Markers; Large Data Sample Model

**Abstract:** Hepatitis B as a serious public health disease, its effective diagnosis and treatment has been the focus of attention. Liver fibrosis and cirrhosis are important diseases of chronic hepatitis B which gradually develop into liver injury. Serious cases can cause malignant diseases such as hepatocellular carcinoma. Therefore, in this context, the early diagnosis and treatment of hepatitis B is extremely important. In order to solve the diagnostic problems of hepatic cirrhosis and liver injury caused by hepatitis B, the diagnostic accuracy of serum model of hepatic fibrosis in the diagnosis of significant cirrhosis and liver injury will be evaluated in detail based on large data samples. Then, based on the analysis of accuracy, the corresponding serological model was selected to select a suitable model for small medical clinics to diagnose hepatitis B, and a non-invasive diagnosis model was proposed to realize the promotion of hepatitis B diagnosis in the context of large data. In the experimental part, the serum markers of hepatitis B cirrhosis and liver injury were screened and analyzed, and the diagnostic serum model of hepatitis B with popularization value was finally selected.

### 1. Introduction

Liver cirrhosis and liver injury are major diseases affecting human public health. There are many pathogenic factors such as alcoholism, schistosomiasis, chemical poisoning, etc. [1-2]. The main pathology of liver cirrhosis and liver injury is that chronic inflammation and necrosis of liver parenchyma can cause abnormal proliferation and deposition of extracellular matrix, and the fibrous connective tissue of liver is relatively or absolutely insufficient [3]. Liver cirrhosis and liver injury are the primary causes of major diseases such as liver cancer. However, it is generally believed that liver cirrhosis and liver injury have the possibility of reversing to normal, but this may be based on early diagnosis [4-5]. Therefore, it is of great significance to study the effective and easy-to-popularize diagnostic techniques of liver cirrhosis and liver injury, which can provide basis for early treatment plan, thus greatly reducing the probability of further deterioration of liver diseases [6-7].

In order to diagnose liver cirrhosis and liver injury in advance, a large number of scholars and research institutions have carried out research and Analysis on it. Some scholars [8-12] have proposed to search for serum markers from the mechanism of the occurrence and development of liver cirrhosis. The markers they seek include interleukin-6, interleukin-8, leptin and other cytokines, which can activate stellate cells. However, the low diagnostic characteristics of this method make it impossible to evaluate the degree of liver cirrhosis independently and accurately. Relevant scholars of Nanjing University [13-16] proposed to diagnose liver cirrhosis and liver injury based on serum microRNAs expression profile. This method improved the accuracy of diagnosis of liver cirrhosis and liver injury to a certain extent, but it is difficult to popularize in community, and the cost of diagnosis is relatively high.

Based on the analysis of the background and research status of hepatitis B cirrhosis and liver injury, and in order to solve the diagnostic problems of hepatitis B-induced cirrhosis and liver injury, this paper will evaluate the diagnostic accuracy of hepatic fibrosis serum model in single and combined diagnosis of significant cirrhosis and liver injury based on large data samples. Then, based on the analysis of accuracy, the corresponding serological model was selected to select a

suiTable model for small medical clinics to diagnose hepatitis B, and finally to achieve the promotion of hepatitis B diagnosis in the context of large data. In the experimental part, the serum markers of hepatitis B cirrhosis and liver injury were screened and analyzed, and the diagnostic serum model of hepatitis B with popularization value was finally selected.

In this paper, the following arrangements are made on the structure of the article: the second section of this paper will specifically analyze the screening and analysis of serum markers of liver cirrhosis and liver injury; the third section of this paper will specifically analyze the value and mechanism of non-invasive diagnostic model of hepatitis B; the fourth section of this paper will carry out experiments for the analysis of the first three sections; finally, this paper will make a summary.

## 2. Screening and analysis of serum markers of liver cirrhosis and liver injury

This section will focus on the screening and analysis of serum markers for large data samples of liver cirrhosis and liver injury. The samples used in this study were serum model samples based on Internet big data technology, and 8 healthy volunteers were included. In the collection and detection of serum samples and acquisition of large data, the main recorded indicators are ALT, AST, HBV serological markers and HBV DNA. In terms of screening criteria, the main criteria are: when the stage of cirrhosis is greater than 2, the default is that there is a significant phenomenon of liver injury. The specific steps for screening serum markers of liver cirrhosis and liver injury are as follows:

### 2.1 Protein screening

The protein screening chip used in this paper is AAH-BLG-1 chip. Firstly, factor detection is carried out based on the chip. The detection factors involved include cytokines, soluble receptors, proteases and angiogenesis factors. Some typical protein names and their sequence are shown in Table 1 below.

Table 1: Typical protein names and sequencing screened by protein screening microarray

1	Angiogenin	Angiopoietin-1	Angiopoietin-2	Angiopoietin-4	6Ckine
2	CNTF	CNTF R alpha	Coagulation Factor III	CRIM 1	CD27/TNFRSF7
3	FGF R4	FGF R5	FGF-4	FGF-5	ErbB3
4	GFR alpha-2	GFR alpha-3	GFR alpha-4	GITR/TNFRF18	GCSF
5	GREMLIN	GRO	GRO-a	Growth Hormone	IL-6
6	IL-5 R alpha	IGF-I SR	IL-6 R	Growth Hormone R	IL-1 SRI
7	Dtk	EDA-A2	EDAR	EDG-1	CXCR-6
8	CCR7	CCR8	CCR9	CD14	BMPR-II

### 2.2 Sample preparation and biotinylation markers

In this step, dialysis of samples, biotinylation labeling of samples and re-dialysis of samples are mainly involved. In the biotinylation labeling of samples, it is necessary to add appropriate dissolved powder to the reagent tubules labeled by rapid centrifugation, blow them repeatedly, mix them fully, and incubate them for 30 minutes at room temperature. In the procedure of sample re-dialysis, dialysis should be done while stirring at a temperature of 4 degrees Celsius, and dialysate replacement should be carried out every 3 hours.

### 2.3 Fluorescence Scanning Detection

In this step, a laser scanner is needed to scan the signal. The green channel is selected for the channel, and the corresponding data is set to PMT: 700. The original data are extracted and

analyzed by the analysis software of laser scanner.

## 2.4 Detection of serum PDGF-BB and macrophage inflammatory protein levels

Enzyme-linked immunosorbent assay (ELISA) was used in this study. Enzyme-linked immunosorbent assay (ELISA) was used to immobilize specific cytokine antibodies at the bottom of the detection pore to form solid-phase carriers. Detailed information of the corresponding kit is shown in Table 2.

Table 2 Detection kits for serum PDGF-BB and macrophage inflammatory protein levels

Microporous plate 96	1
Concentrated cleaning solution	30mL
Sample diluent	2
TMB Labeled One Step Display Agent	25mL
Termination fluid	200uL
Antibody to be tested in termination solution	2*10mL

## 2.5 Selection of Serum Samples

The information of serum samples collected above is stored in cloud database, and the serum samples are screened and labeled from the database. When establishing SPSS18.0 database, we need to process the detected serum sample model and draw the related statistical map. At the same time, Ko-Sm method is used to test the corresponding data to check whether it conforms to the normal distribution. According to the normal distribution, the mean or median values were used to describe the variables, and t-test or Mann-Whitney U-test was used to compare the differences between the serum model groups. Based on this database, 12 typical serum model data were screened as follows:

Table 3 Data Table of 12 typical serum models of hepatitis B cirrhosis and liver injury

index	CHB(6)	Cirrhosis(6)
age	50	45
Gender (male ratio)	100%	75%
ALB	47.1	40.4
TBIL	13.9	24.5
ALP	99.8	134.9
GGT	22.9	41.2
ALT	29.7	33.2

Based on the above screening steps and the typical hepatitis B serum model, we can get the corresponding cytokine diagnostic effect of significant cirrhosis. Based on ROC curve, serum PDGF level was described to diagnose significant cirrhosis and liver injury. The corresponding curve is shown in Fig. 1, in which the corresponding PDGF level is positively correlated with cirrhosis, that is, the higher the PDGF level is, the more significant the corresponding cirrhosis is. The influence curves of MIP and TGF on liver cirrhosis are also described in Figure 1.

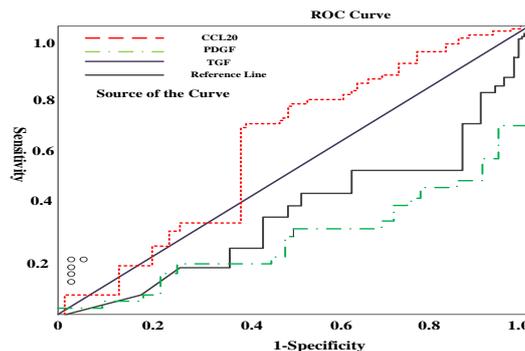


Figure 1 Descriptive curve of PDGF and other cytokines on the degree of liver cirrhosis

### 3. The mechanism of noninvasive diagnostic model of hepatitis B

In this section, we will design a non-invasive diagnostic model of hepatitis B based on the screened hepatitis B serum model in the second section and analyze its value and mechanism.

The non-invasive diagnostic model relies mainly on the synthesis of the hepatitis B cirrhosis model. The corresponding calculation model rules are shown in Table 4 below. It can be seen from the Table that the corresponding basic non-invasive models are AAR, GPRI, S-index, APRI, FIB-4, Fibro-Q and the corresponding API. The corresponding ALB represents albumin, the corresponding ALT represents alanine aminotransferase, the corresponding AST represents glutathione aminotransferase, the corresponding GGT represents glutamyl transpeptidase, and the corresponding INR is the international standardized ratio of prothrombin. The corresponding PLT is platelet and the corresponding ULN is the upper limit of normal value.

Table 4 The basic model of non-invasive hepatitis B model proposed in this paper

Noninvasive model of liver cirrhosis	Computational formulas
AAR	AST/ALT
GPRI	GGT/PLT
S-index	$1 * GGT / [PLT] * 100$
APRI	$[age * AST] / [PLT * ALT]$
FIB-4	$[AST * INR] / [PLT * ALT]$
Fibro-Q	$[age * AST] / [PLT * ALT]$
API	$[age * AST] / [PLT * ALT]$

Based on the above seven models, the hardness of liver cirrhosis was analyzed by ROC, and the analysis was used as the diagnostic basis of non-invasive liver cirrhosis diagnosis model. In this paper, SPSS18.0 statistical software is used in the actual non-invasive diagnosis. Based on the analysis software, the ROC curve is plotted in the horizontal and vertical coordinates of the true and false positive rates of hepatitis B. The corresponding curve is shown in Figure 2. The corresponding LSM, S-index, GPRI, FIB-4, APRI, API and Fibro-Q are 0.757, 0.726, 0.726, 0.621, 0.619, 0.569 and 0.495, respectively.

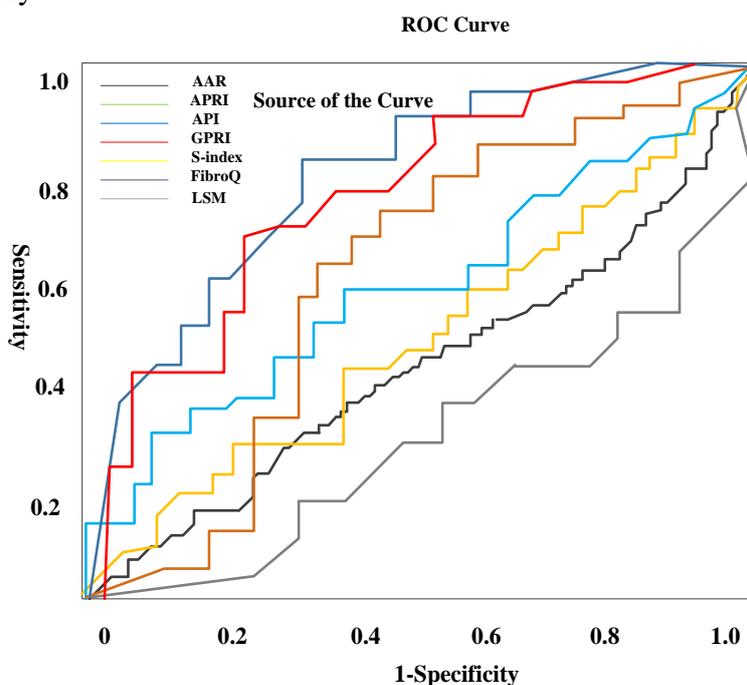


Figure 2 ROC curve of noninvasive serum model for diagnosis of liver cirrhosis and liver injury

The corresponding ROC liver cirrhosis and liver injury serum model diagnoses significant cirrhosis AUROCs as shown in Table 5.

Table 5 Serum model of ROC cirrhosis and liver injury for diagnosis of significant cirrhosis AUROCs

model	AUROC	Standard error	P value	95%Ci
LSM	0.757	0.037	0.034	0.69
S index	0.726	0.037	0.033	0.663
GPRI	0.726	0.032	0.031	0.550
FIB-4	0.621	0.035	0.035	0.66
APRI	0.619	0.037	0.037	0.508
API	0.681	0.037	0.034	0.671
Fibro-Q	0.671	0.031	0.045	0.496
AAR	0.456	0.037	0.036	0.421

#### 4. Experimental analysis

In order to verify the effectiveness of the diagnostic model proposed in this paper in the diagnosis of liver cirrhosis, serum MIP diagnostic significance test was carried out, in which ROC curve was used to analyze, and the hardness of serum under three cytokines MIP, PDGF and TGF was evaluated based on the area under the curve. The corresponding detection results are shown in Figure 3. It can be found that MIP has a significant role in the diagnosis of liver cirrhosis, while the corresponding PDFG-BB and TGF have a positive correlation with the severity of liver cirrhosis, but the specific correlation value can not be detected.

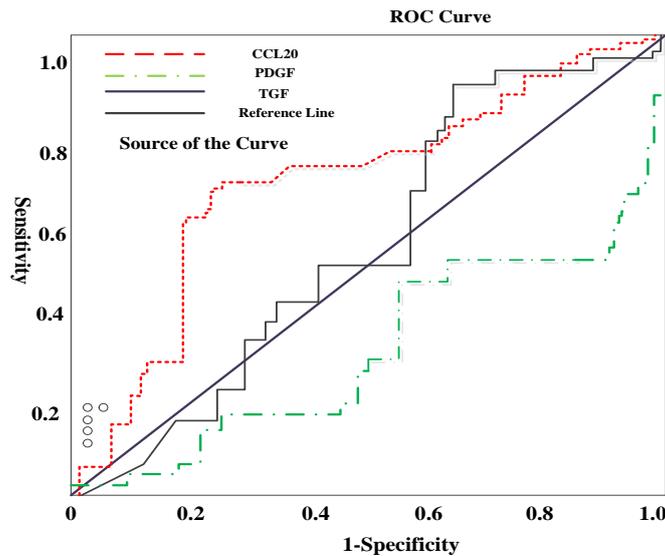


Figure 3 ROC graphics under the diagnostic model presented in this paper

#### 5. Conclusion

This paper mainly focuses on the analysis of diagnostic models of liver cirrhosis and liver injury, a worldwide health problem. In order to detect and accurately diagnose the severity of liver cirrhosis and liver injury in advance, the diagnostic accuracy of liver fibrosis serum model in the diagnosis of significant cirrhosis and liver injury was assessed in detail based on large data samples. Then, based on the analysis of accuracy, the corresponding serological model was selected to select a suitable model for small medical clinics to diagnose hepatitis B, and a non-invasive diagnosis model was proposed to realize the promotion of hepatitis B diagnosis in the context of large data. In the experimental part, the serum markers of hepatitis B cirrhosis and liver injury were screened and analyzed, and the diagnostic serum model of hepatitis B with popularization value was finally selected.

## References

- [1] Wu T, Li J, Shao L, et al. Development of diagnostic criteria and a prognostic score for hepatitis B virus-related acute-on-chronic liver failure[J]. *Gut*, 2018, 67(12):2181.
- [2] Wei B, Feng S, Chen E, et al. M2BPGi as a potential diagnostic tool of cirrhosis in Chinese patients with Hepatitis B virus infection.[J]. *Journal of Clinical Laboratory Analysis*, 2018, 32(2):e22261.
- [3] Huang X W, Liao B, Huang Y, et al. Non-Invasive Diagnostic Criteria for Hepatocellular Carcinoma in Hepatitis B Virus-Endemic Areas: Is Cirrhosis Indispensable?[J]. *Digestive Diseases*, 2018, 36(3).
- [4] Hong Z, Chen M, Lu S, et al. Metabolic characterization of hepatitis B virus-related liver cirrhosis using NMR-based serum metabolomics[J]. *Metabolomics*, 2017, 13(10):121.
- [5] Chen S, Chen H, Gao S, et al. Differential expression of plasma microRNA - 125b in hepatitis B virus - related liver diseases and diagnostic potential for hepatitis B virus - induced hepatocellular carcinoma[J]. *Hepatology Research*, 2017, 47(4):312.
- [6] Yip C F, Chan L Y, Tse Y K, et al. On-Treatment Improvement of MELD Score Reduces Death and Hepatic Events in Patients With Hepatitis B-Related Cirrhosis[J]. *American Journal of Gastroenterology*, 2018, 113.
- [7] Chang F M, Wang Y P, Lang H C, et al. Statins decrease the risk of decompensation in hepatitis B virus- and hepatitis C virus-related cirrhosis: A population-based study.[J]. *Hepatology*, 2017, 66(3).
- [8] Shim J J, Oh C H, Kim J W, et al. Liver cirrhosis stages and the incidence of hepatocellular carcinoma in chronic hepatitis B patients receiving antiviral therapy[J]. *Scandinavian Journal of Gastroenterology*, 2017, 52(9):1.
- [9] Li J, Guo Q J, Cai J Z, et al. Simultaneous liver, pancreas-duodenum and kidney transplantation in a patient with hepatitis B cirrhosis, uremia and insulin dependent diabetes mellitus[J]. *World Journal of Gastroenterology*, 2017, 23(45):8104-8108.
- [10] Wang Y, Xiong J, Niu M, et al. Statins and the risk of cirrhosis in hepatitis B or C patients: a systematic review and dose-response meta-analysis of observational studies[J]. *Oncotarget*, 2017, 8(35).
- [11] Zhang H, Yan X L, Guo X X, et al. MiR-27a as a predictor for the activation of hepatic stellate cells and hepatitis B virus-induced liver cirrhosis:[J]. *Oncotarget*, 2018, 9(1):1075-1090.
- [12] Wang M, Wei C, Shi Z, et al. Study on the diagnosis of small hepatocellular carcinoma caused by hepatitis B cirrhosis via multi-slice spiral CT and MRI[J]. *Oncology Letters*, 2018, 15(1):503.
- [13] Pu K, Shi J H, Wang X, et al. Diagnostic accuracy of transient elastography (FibroScan) in detection of esophageal varices in patients with cirrhosis: A meta-analysis[J]. *World Journal of Gastroenterology*, 2017, 23(2):345-356.
- [14] Coppola N, Alessio L, Gualdieri L, et al. Hepatitis B virus infection in undocumented immigrants and refugees in Southern Italy: demographic, virological, and clinical features:[J]. *Infectious Diseases of Poverty*, 2017, 6(1):33.
- [15] Wang J, Yan X, Yang Y, et al. A novel predictive model using routinely clinical parameters to predict liver fibrosis in patients with chronic hepatitis B[J]. *Oncotarget*, 2017, 8(35):59257-59267.
- [16] Fernández Carrillo C, Lens S, Llop E, et al. Treatment of hepatitis C virus infection in patients with cirrhosis and predictive value of model for end - stage liver disease: Analysis of data from the Hepa - C registry[J]. *Hepatology*, 2017, 65(6):1810-1822