# Predictive value of liver and spleen stiffness measurement based on two-dimensional shear wave elastography for the portal vein pressure in patients with compensatory viral cirrhosis

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**Objective:** This study aimed to explore the predictive value of liver and spleen stiffness measurement based on two-dimensional shear wave elastography for the portal vein pressure in patients with compensatory viral cirrhosis. **Methods:** 107 patients with compensatory viral cirrhosis and 76 patients with viral hepatitis from January 2017 to August 2019 were included as cirrhosis group and hepatitis group. Patient data were obtained during admission, and this study was a review and analysis of patient data. Liver stiffness measurement (LSM), spleen stiffness measurement (SSM), portal vein diameter and spleen thickness were compared between the two groups, and their diagnostic value for compensatory viral cirrhosis was analyzed. According to the hepatic vein pressure, the cirrhosis group patients were divided into non-hypertensive group (no portal hypertension, Hepatic Venous Pressure Gradient (HVPG) < 5 mmHg), mild group (mild portal hypertension, 5 mmHg ≤ HVPG ≤ 10 mmHg) and severe group (clinically significant portal hypertension group, HVPG > 10 mmHg). LSM, SSM, portal vein diameter and spleen thickness of the three groups were compared, and the correlation between SSM and hepatic vein pressure was analyzed. **Results:** The LSM, SSM, portal vein diameter and spleen thickness in cirrhosis group were higher than those in hepatitis group (all $P<0.05$); AUC of combined detection in the diagnosis of liver cirrhosis was greater than that of LSM, SSM and spleen thickness detection alone (all $P<0.05$); LSM, SSM, portal vein diameter and spleen thickness increased with the increase of hepatic vein pressure in patients with liver cirrhosis (all $P<0.05$); LSM, SSM, portal vein diameter and spleen thickness were all positively correlated with hepatic vein pressure ($P<0.05$); ROC curve showed that AUC of combined detection in the diagnosis of clinically significant portal hypertension was greater than that of LSM, SSM, portal vein diameter and spleen thickness alone (all $P<0.05$); The increase of LSM, SSM, portal vein diameter and spleen thickness were the influencing factors of the increase of hepatic vein pressure (all P<0.05). **Conclusion**:

There was an increase of LSM and SSM in patients with compensatory viral cirrhosis, which were positively correlated with hepatic venous pressure, and combined index detection has diagnostic and predictive value for the change of portal venous pressure.

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## Abstract

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**Methods:** 107 patients with compensatory viral cirrhosis and 76 patients with viral hepatitis from January 2017 to August 2019 were included as cirrhosis group and hepatitis group. Patient data were obtained during admission, and this study was a review and analysis of patient data. Liver stiffness measurement (LSM), spleen stiffness measurement (SSM), portal vein diameter and spleen thickness were compared between the two groups, and their diagnostic value for compensatory viral cirrhosis was analyzed. According to the hepatic vein pressure, the cirrhosis group patients were divided into non-hypertensive group (no portal hypertension, Hepatic Venous Pressure Gradient (HVPG) < 5 mmHg), mild group (mild portal hypertension, 5 mmHg ≤ HVPG ≤ 10 mmHg) and severe group (clinically significant portal hypertension group, HVPG > 10 mmHg). LSM, SSM, portal vein diameter and spleen thickness of the three groups were compared, and the correlation between SSM and hepatic vein pressure was analyzed.

**Results:** The LSM, SSM, portal vein diameter and spleen thickness in cirrhosis group were higher than those in hepatitis group (all $P<0.05$); AUC of combined detection in the diagnosis of liver cirrhosis was greater than that of LSM, SSM and spleen thickness detection alone (all $P$

<0.05); LSM, SSM, portal vein diameter and spleen thickness increased with the increase of hepatic vein pressure in patients with liver cirrhosis (all $P$ <0.05); LSM, SSM, portal vein diameter and spleen thickness were all positively correlated with hepatic vein pressure ($P$ <0.05); ROC curve showed that AUC of combined detection in the diagnosis of clinically significant portal hypertension was greater than that of LSM, SSM, portal vein diameter and spleen thickness alone (all $P$<0.05); The increase of LSM, SSM, portal vein diameter and spleen thickness were the influencing factors of the increase of hepatic vein pressure (all P<0.05).

**Conclusion**: There was an increase of LSM and SSM in patients with compensatory viral cirrhosis, which were positively correlated with hepatic venous pressure, and combined index detection has diagnostic and predictive value for the change of portal venous pressure.

**Keywords:** compensatory viral cirrhosis; two-dimensional shear-wave elastic imaging; liver and spleen stiffness; portal vein pressure; correlation; predictive value

## 0 Introduction

Liver cirrhosis is the late stage of many liver diseases. It has no typical clinical manifestations in the compensatory stage during the course of disease, but it can be manifested as ascites, esophageal and gastric variceal bleeding and other complications in the decompensated stage. Portal hypertension is the main complication of liver cirrhosis. Most of the normal liver blood supply comes from the portal vein. The anatomical structure of the portal vein is relatively special. Both the beginning and end of the portal vein are capillaries. When the degree of liver cirrhosis is aggravated, the blood vessels in the liver parenchyma gradually become thinner, and the pressure of the portal vein increases, forcing a large number of portal vein blood to reverse flow and enter the collateral circulation, resulting in esophageal and gastric varices, which affects the prognosis of patients [1-2]. At present, the measurement of hepatic vein pressure gradient is often used to assess the severity of portal hypertension, but it is an innovative operation with high limitations. Ultrasonic elastic imaging is an inspection technology developed based on two-dimensional ultrasound. The probe is used to compress the tissue longitudinally, and the longitudinal strain force is generated inside the tissue. Due to the uneven elastic distribution inside the tissue, the strain force will be different, so the internal situation of the tissue can be evaluated [3-4]. Two-dimensional shear wave elastic imaging is the latest elastic imaging technology. It estimates the tissue hardness by measuring the propagation

velocity of elastic shear wave in the tissue. Compared with ultrasonic elastic imaging, it has evident advantages. It can perform elastic imaging on the basis of two-dimensional images. It does not need to apply pressure during operation. It can observe the two-dimensional images in real time with avoiding the pipeline structure in the tissue. The elastic modulus value is measured in full quantity. Thus, it can be used to judge the degree of tissue lesions [5-6]. Based on this, this study aimed to explore the predictive significance of liver and spleen stiffness measurement based on two-dimensional shear wave elastography for the changes of portal vein pressure in patients with compensatory viral cirrhosis, and to provide a reference basis for the development of assessment methods of portal vein pressure changes.

# 1 Materials & Methods

## 1.1 Clinical data

From January 2017 to August 2019, 107 patients with compensatory viral cirrhosis and 76 patients with viral hepatitis were taken as cirrhosis group and hepatitis group, respectively. There were no significant differences in general data between the two groups (all $P>0.05$, Table 1). The study was approved by the Institutional Review Board and Research Ethics Committee of the No.2 People's Hospital of Lanzhou, and was conducted in accordance to the tenets of the Declaration of Helsinki and the ethical approval of No.2 People's Hospital of Lanzhou agreed to waive the informed consent.

## 1.2 inclusion criteria

Patients (1) who met the diagnostic criteria for viral hepatitis or cirrhosis [7-8]; (2) with complete clinical data; (3) Two-dimensional shear wave elastography examination was performed.

## 1.3 Exclusion criteria

(1) Patients with cirrhosis caused by other reasons; (2) patients complicated with hepatocellular carcinoma, portal vein thrombosis and other serious complications; (3) patients with splenic lesions;(4) patients complicated with blood diseases; (5) Patients with connective tissue diseases; (6) patients with active infectious diseases.

## 1.4 Methods

### 1.4.1 Two-dimensional shear-wave elastography examination

Real-time shear-wave elastography of liver was performed on all patients using supersonic imagine aixplorer machine and SC6-1 abdominal probe. The patient was placed in a supine position and his right upper limb was raised and placed on his head, fully exposing the right abdomen. Two-dimensional ultrasonography was performed on the right axillary front to the midaxillary line between the 4th and 7th ribs. The coupling agent was evenly applied on the skin surface with avoiding the thick pipe structures such as hepatic blood vessels and bile ducts and the location of gallbladder. The probe was vertical to the skin. After the 2D image was clearly displayed, the machine was switched to SWE mode. The sampling frame range was 4cm*3cm, the area of interest was set to 20.0 mm, and the elastic measurement SCALE was set to 40 kPa. Liver parenchyma about 2 cm below the capsule of the right lobe of liver was selected as the upper edge. Patients were asked to hold their breath for 3 to 5 s in a calm state, and the measurement was considered successful if the color of the sample box was more than 90% full. The region with relatively uniform image color was selected for detection, and the average value of elastic modulus in the detection region was displayed. It was detected for 5 times in total and the average value was taken as LSM. SSM detection: The patient was placed in the right decubitus position, with the left arm fully extended up and placed on the top of the head. The left midline or the posterior axillary line between the 9th and 11th ribs was selected. The probe was placed in the thickest middle part of the spleen, and the sampling range was set to 4cm*3cm. The spleen parenchyma about 1 cm below the capsule was selected as the upper margin, and the area of interest was 20.0 mm. The elastic measurement SCALE was 70 kPa. The measurement method was the same as that of LSM.

**1.4.2 Portal vein diameter and spleen thickness examination**

Philips EPIQ5 and Mindray M5 color Doppler ultrasound diagnostic instrument with probe frequency of 3-9 MHz were applied. The patient was placed in supine position with his hands raised above his head. When scanning was not satisfactory, the position of the patient could be changed appropriately and his breathing should be maintained smoothly. The longitudinal section of the first porta hepatis under the right costal margin was taken as the standard measurement section. The examination showed that the common bile duct was full length and posterior to the head of pancreas. The portal vein was measured at 1~2 cm from the first hilum. The splenic hilum and splenic vein were shown by scanning along the intercostal oblique

section. The diameter line from the hilum to the opposite side of the spleen was measured as the thickness of the spleen.

**1.4.3 Hepatic vein pressure gradient detection**

Before examination, the necessity and risks of hepatic venous pressure testing should be explained to patients and their families, and the testing can be carried out only after signing the informed letter of interventional diagnosis and treatment. Patients were instructed to take supine position and turn their head to the opposite side of puncture as far as possible. The right internal jugular vein was selected as puncture point, and local anesthesia was performed with 2% lidocaine. After successful puncture of the right internal jugular vein with the Seldinger technique, the 5F venipecture sheath (TERUMO, Japan) was inserted with the guide wire. The Cordis 5F multifunctional angiography catheter (Cordis, USA) was inserted into the main right hepatic vein under X-ray fluoroscopy. After successful introduction was confirmed by angiography by infusion of 2 mL iohexol, the automatic manometer was connected to read the pressure data, namely, the free hepatic venous pressure (FHVP). Guided by the guide wire, the multifunctional catheter was continued to reach the end of the hepatic vein, and 2 mL iodihyl was injected to confirm the angiography. The pressure data at this time was read, namely, the wedged hepatic venous pressure (WHVP). The difference of the two was the hepatic venous pressure gradient (HVPG). According to the hepatic venous pressure, the cirrhosis group was divided into the non-hypertension group (no portal hypertension, HVPG $< 5$ mmHg), the mild group (mild portal hypertension group, 5 mmHg $\leq$ HVPG $\leq$ 10 mmHg), and the severe group (clinically significant portal hypertension group, HVPG $> 10$ mmHg).

**1.5 Observation Indicators: Baseline data, LSM, SSM, portal vein diameter and spleen thickness of patients with cirrhosis and hepatitis were collected**

(1) LSM, SSM, portal vein diameter and spleen thickness were compared between the cirrhosis group and the hepatitis group, and their diagnostic value for compensatory viral cirrhosis was analyzed. (2) LSM, SSM, portal vein diameter and spleen thickness of the non-hypertension group, mild group and severe group were compared, and the correlation between each index and hepatic vein pressure as well as the diagnostic value of clinically significant portal vein hypertension were analyzed.

**1.6 Statistical treatment**

SPSS22.0 software was used to process the data. The counting data were expressed as %, and the difference between groups was compared by $\chi^2$ test. The measurement data were expressed by ( $\bar{x} \pm$ S) after normal test, and the difference between groups was compared by *t* test. ROC curve was used to analyze the diagnostic value of LSM, SSM, portal vein diameter and spleen thickness for compensatory viral cirrhosis. Spearman test was used to analyze the correlation between LSM, SSM, portal vein diameter, spleen thickness and hepatic vein pressure. Logistic regression was used to analyze the correlation of LSM, SSM, portal vein diameter and spleen thickness with clinically significant portal hypertension. $P<0.05$ meant the difference was statistically significant.

## 2 Results

### 2.1 Comparison of LSM, SSM, portal vein diameter and spleen thickness between cirrhosis group and hepatitis group

The values of LSM, SSM, portal diameter and spleen thickness in cirrhosis group were all higher than those in hepatitis group (all $P<0.05$, Figure 1).

### 2.2 Diagnostic value of LSM, SSM, portal vein diameter and spleen thickness for cirrhosis

The AUC of combined detection was greater than that of LSM, SSM and spleen thickness alone (all $P<0.05$, Table 2 and Figure 1).

### 2.3 Comparison of LSM, SSM, portal diameter and spleen thickness in patients with different hepatic venous pressures

LSM, SSM, portal vein diameter and spleen thickness increased with the increase of hepatic vein pressure (all P<0.05, Figure 3).

### 2.4 Correlation analysis of LSM, SSM, portal vein diameter and spleen thickness with hepatic vein pressure

LSM, SSM, portal vein diameter and spleen thickness were positively correlated with hepatic vein pressure (all $P<0.05$, Figure 4).

### 2.5 Diagnostic value analysis of LSM, SSM, portal vein diameter and spleen thickness for clinically significant portal hypertension

ROC curve showed that AUC of combined detection was greater than that of SSM, portal diameter and spleen thickness detection alone (all $P< 0.05$, Table 3 and Figure 5).

### 2.6 Logistic regression analysis of LSM, SSM, portal vein diameter and spleen thickness with increased hepatic vein pressure

The increase of LSM, SSM, portal vein diameter and spleen thickness were the influencing factors for the increase of hepatic vein pressure (all $P< 0.05$, Table 4).

## Discussion

Portal hypertension is the main cause of esophageal and gastric varices rupture and bleeding and death in patients with cirrhosis. Clinical data show that portal hypertension is a common complication in patients with cirrhosis, which can cause ascites, varicose esophagogastric fundus and splenomegaly, and can lead to death in severe cases [9]. It has also been reported that the degree of portal hypertension is closely related to the severity of liver disease both functionally and histologically [10-11]. HVPG is the gold standard for the diagnosis of portal hypertension, which can reflect the severity of the disease and the prognosis of patients. However, it is an invasive examination with high requirements on medical conditions, professional level of operators and postoperative patient care [12]. Ultrasonic shear wave elastography is a non-invasive ultrasonic quantitative evaluation technology. By generating shear waves that can propagate in human tissues and receiving reflected echoes, the propagation speed of shear waves in tissues is detected to reflect the hardness of tissues. The greater the hardness of tissues, the faster the propagation speed of shear waves is. For another thing, compared with conventional ultrasound elastography, two-dimensional shear wave elastography is less susceptible to obesity, ascites and other factors, and can better reflect the real situation of tissue elasticity, and makes up for the shortcomings of acoustic radiation force pulse imaging, which can only detect tissue elasticity near the focal point due to limited sampling area [13-14]. Relevant reports indicate that two-dimensional shear wave elastography can mark the elasticity of different tissues in different colors to reflect the hardness of liver and spleen [15]. The results of the present study showed that LSM and SSM values, portal vein diameter and spleen thickness in the cirrhosis group were higher than those in the hepatitis group, indicating that LSM, SSM and portal vein diameter and spleen thickness were increased in the cirrhosis patients. This was mainly because the spleen position was close to the body surface, and shear wave elastic imaging could obtain reliable spleen hardness values. The splenic vein and portal vein continue behind the pancreatic neck, and when portal vein hypertension occurs, the splenic vein blood flow is blocked, leading to

changes in the spleen, such as sinus congestion and parenchymal fibrosis, and further changes in the morphology of liver and spleen [16]. In addition, this study found that the AUC of SSM, portal vein diameter and spleen thickness combined detection in the diagnosis of cirrhosis was greater than 0.9, indicating that the combined detection of all indicators has differentially diagnostic value for cirrhosis and hepatitis, and it may be applied in the early diagnosis of cirrhosis.

Portal hypertension is the main factor of esophageal and gastric variceal bleeding and rupture and death in patients with cirrhosis. Portal hypertension is closely related to the severity of liver disease both functionally and histologically. Therefore, the detection of portal venous pressure is of vital importance to evaluate the severity and prognosis of cirrhosis patients [17-18]. Relevant studies indicate that portal hypertension not only causes splenomegaly, but also changes in splenic blood flow, tissue hyperplasia and fibrosis [19-20]. The hardness of liver and spleen can reflect the degree of liver lesions to a certain extent, and liver portal hypertension is closely related to the degree of cirrhosis, suggesting that liver and spleen hardness may be related to liver portal hypertension [23-24]. The present study found that LSM, SSM, portal vein diameter and spleen thickness were positively correlated with hepatic vein pressure, indicating that the higher the hepatic vein pressure, the greater the hardness of liver and spleen. The reason is that, with the progression of cirrhosis, the viscera is in a high circulation state, and the congestion of liver and spleen is aggravated; In addition, the establishment of collateral circulation of portal body changes the hemodynamics of liver and spleen, leading to the increase of hardness of liver and spleen [25]; The splenic vein and portal vein continue behind the pancreatic neck, and when portal vein hypertension occurs, the splenic vein blood flow is blocked, resulting in the splenic sinus congestion and expansion and therefore the change of spleen thickness [26-27]. Further analysis found that the increase of LSM, SSM, portal vein diameter and spleen thickness were the influencing factors of the increase of hepatic vein pressure, indicating that the increase of liver and spleen stiffness and the thickening of spleen were the influencing factors of the increase of hepatic vein pressure. This is mainly because in the process of liver fibrosis, liver stiffness increases and intrahepatic vascular resistance increases, resulting in increased hepatic venous pressure [28-30]. In our study, it was found that AUC of the combined detection of AUC, SSM, portal diameter and spleen thickness of clinically

significant portal hypertension was greater that of measured separately, indicating that combined detection of all indicators has diagnostic value for portal hypertension.

## Conclusions

The increase of LSM and SSM in patients with compensatory viral cirrhosis is positively correlated with hepatic vein pressure, and the combined detection of LSM and SSM has diagnostic and predictive value for changes in portal vein pressure.

## Acknowledgements

Not applicable.

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Figure 1 Comparison of LSM, SSM, portal vein diameter and spleen thickness between cirrhosis group and hepatitis group.
(Note: Compared with the cirrhosis group, *$P$<0.05).

Figure 2 ROC curves of LSM, SSM, portal vein diameter and spleen thickness in differentiating hepatitis and cirrhosis.

Figure 3 Comparison of LSM, SSM, portal vein diameter and spleen thickness in patients with different hepatic vein pressures.
(Note: All the comparisons of LSM, SSM, portal vein diameter and spleen thickness in patients with different hepatic venous pressure showed P<0.05).

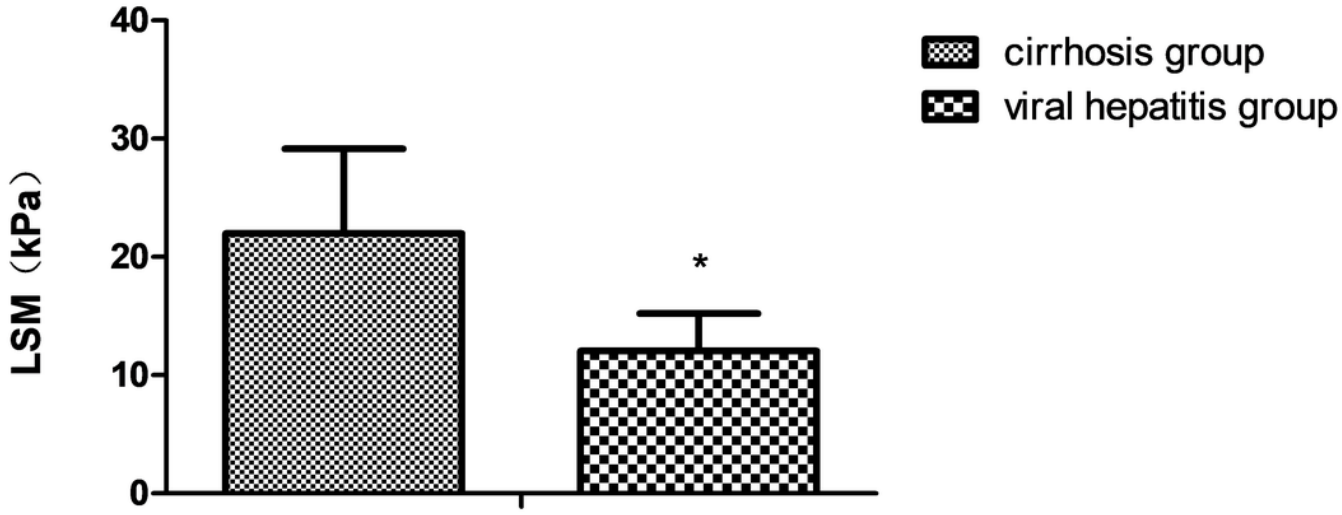
Figure 4 Correlation analysis of LSM, SSM, portal vein diameter and spleen thickness with hepatic vein pressure.

Figure 5 Diagnostic value analysis of LSM, SSM, portal vein diameter and spleen thickness for clinically significant portal hypertension.

# Figure 1

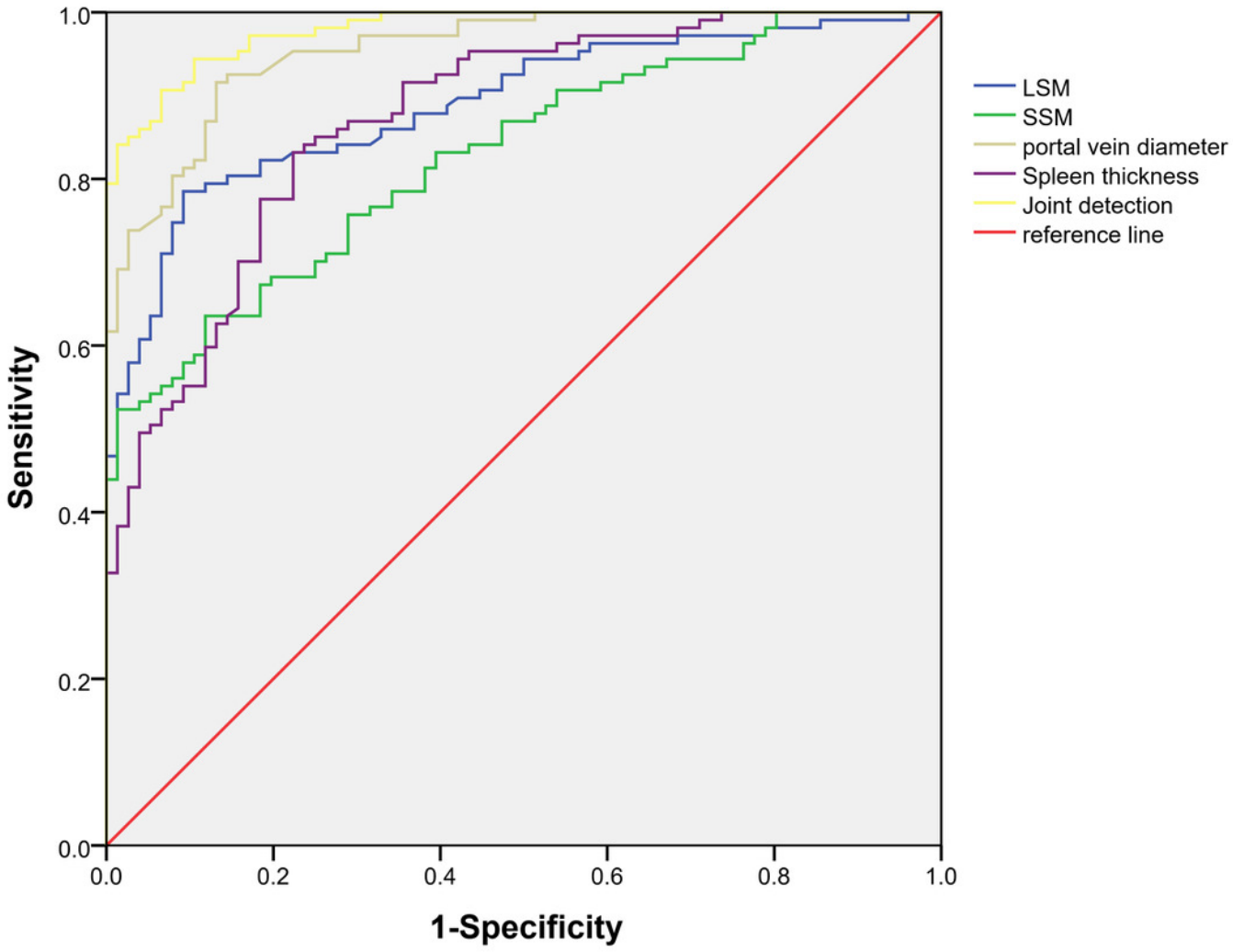
Comparison of LSM, SSM, portal vein diameter and spleen thickness between cirrhosis group and hepatitis group.

Note: Compared with the cirrhosis group, *$P$<0.05



# Figure 2

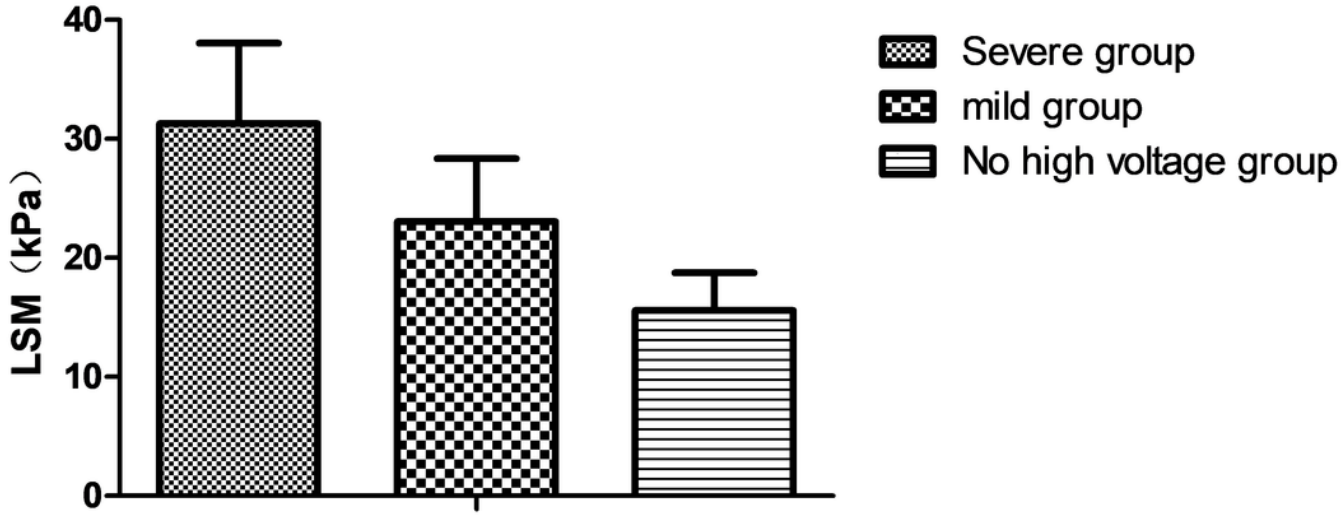
ROC curves of LSM, SSM, portal vein diameter and spleen thickness in differentiating hepatitis and cirrhosis



# Figure 3

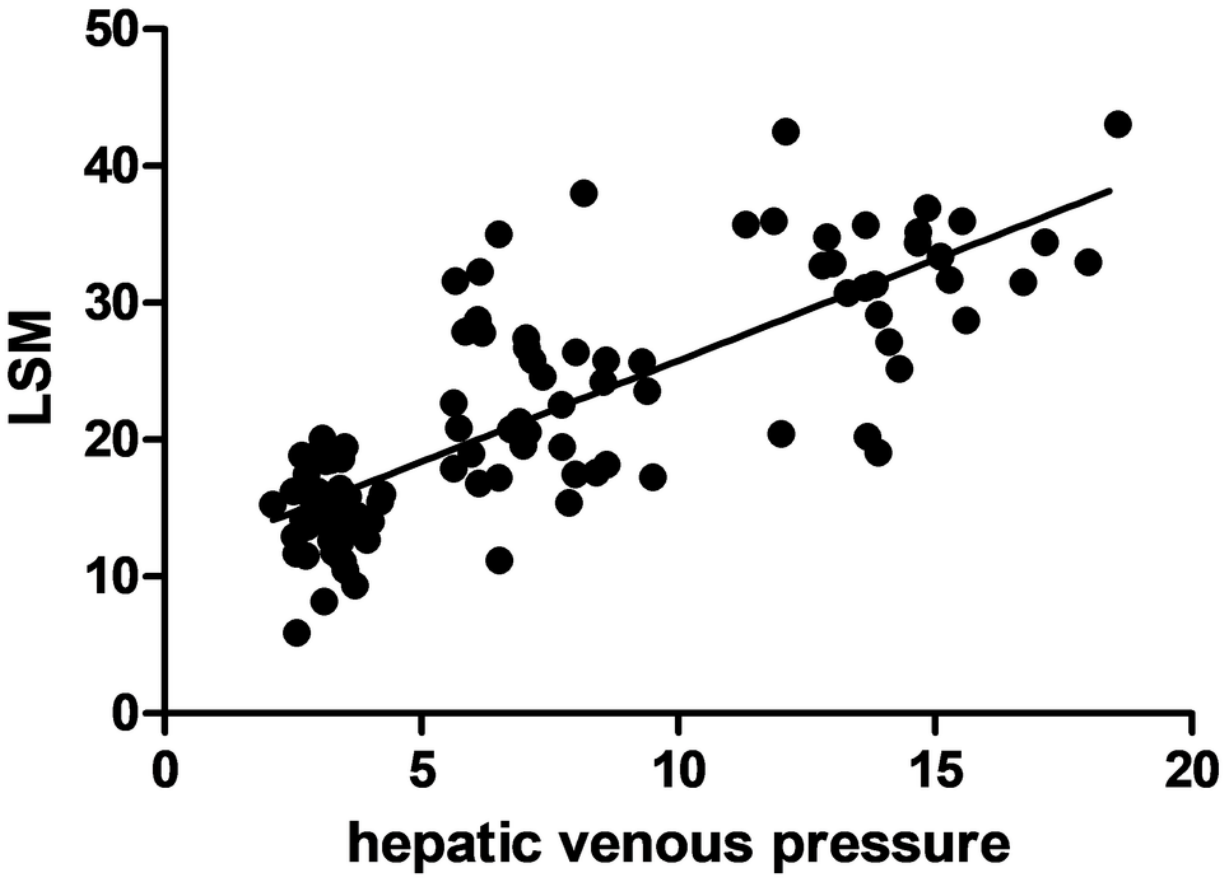
Comparison of LSM, SSM, portal vein diameter and spleen thickness in patients with different hepatic vein pressures

Note: All the comparisons of LSM, SSM, portal vein diameter and spleen thickness in patients with different hepatic venous pressure showed $P<0.05$



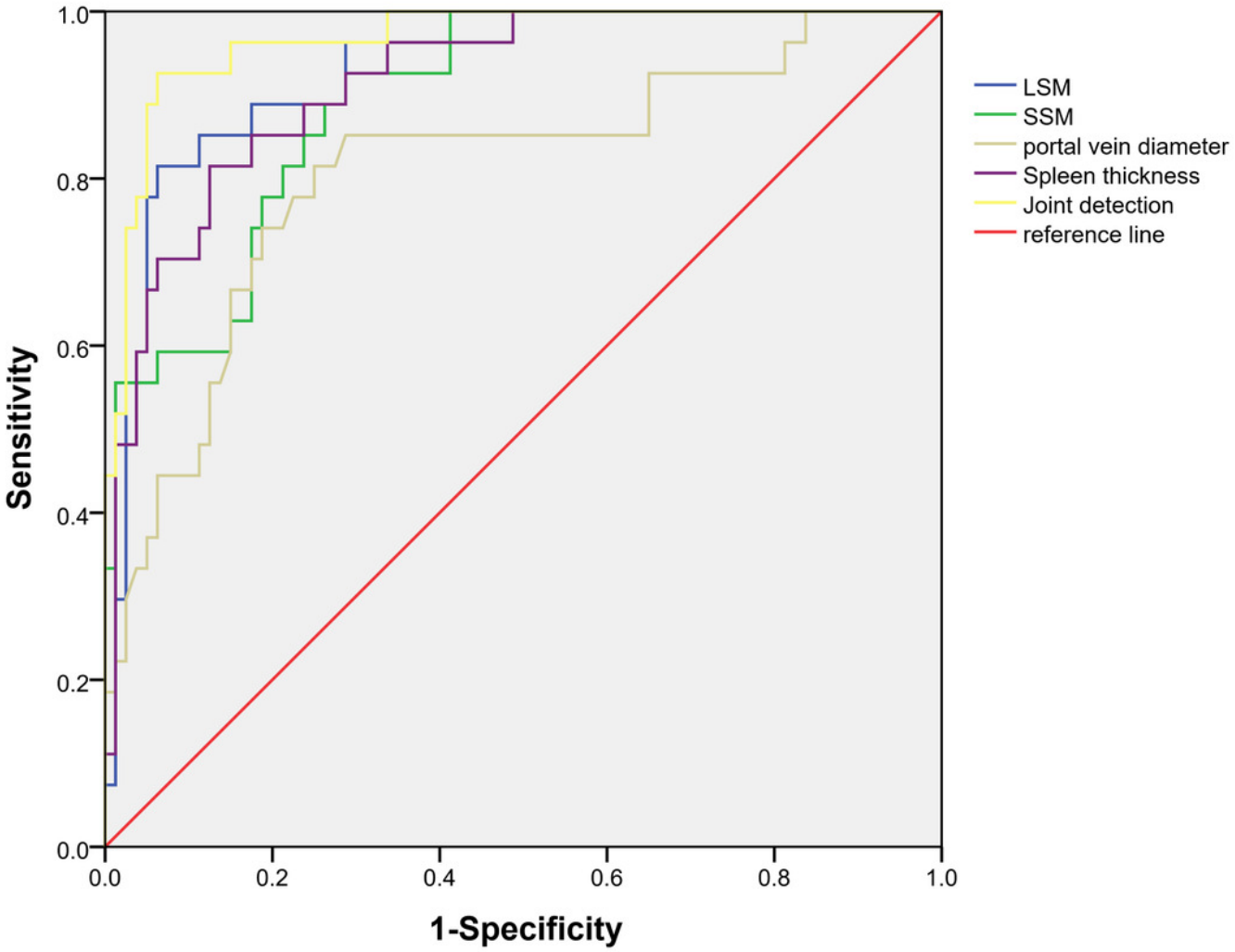
# Figure 4

Correlation analysis of LSM, SSM, portal vein diameter and spleen thickness with hepatic vein pressure



# Figure 5

Diagnostic value analysis of LSM, SSM, portal vein diameter and spleen thickness for clinically significant portal hypertension



## Table 1(on next page)

Comparison of general data between cirrhosis group and hepatitis group

1 Table 1 Comparison of general data between cirrhosis group and hepatitis group

| General data | Cirrhosis group (n=107) | Hepatitis group (n=76) | $\chi^2/t$ | *P* |
|---|---|---|---|---|
| Gender (cases) | | | 0.625 | 0.429 |
| Male | 64 | 41 | | |
| Female | 43 | 35 | | |
| Age (years) | 53.52±5.16 | 54.87±5.59 | 1.685 | 0.094 |
| Course of disease (years) | 4.09±0.63 | 3.98±0.61 | 1.179 | 0.240 |
| BMI ($kg/m^2$) | 23.18±2.52 | 23.51±2.73 | 0.843 | 0.400 |
| Complicated underlying diseases | | | | |
| Hyperlipidemia | 31 | 18 | 0.634 | 0.426 |
| Hypertension | 19 | 12 | 0.122 | 0.727 |
| Coronary heart disease | 10 | 5 | 0.452 | 0.501 |

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## Table 2(on next page)

Diagnostic value of LSM, SSM, portal vein diameter and spleen thickness for cirrhosis

Note: Compared with combination, *$P<0.05$

Table 2 Diagnostic value of LSM, SSM, portal vein diameter and spleen thickness for cirrhosis

| Indicator | Cutoff value | AUC | SE | 95%CI |
|---|---|---|---|---|
| LSM | 16.52kPa | 0.889* | 0.024 | 0.843~0.935 |
| SSM | 35.59kPa | 0.827* | 0.029 | 0.770~0.884 |
| Portal vein diameter | 11.24cm | 0.954 | 0.013 | 0.928~0.980 |
| Spleen thickness | 109.37cm | 0.872* | 0.026 | 0.822~0.922 |
| Combination | | 0.979 | 0.008 | 0.964~0.994 |

Note: Compared with combination, *$P<0.05$.

## Table 3(on next page)

Diagnostic value analysis of LSM, SSM, portal vein diameter and spleen thickness for clinically significant portal hypertension

Note: Compared with combination, *$P$<0.05.

Table 3 Diagnostic value analysis of LSM, SSM, portal vein diameter and spleen thickness for clinically significant portal hypertension

| Indicator | Cutoff value | AUC | SE | 95%CI |
|---|---|---|---|---|
| LSM | 27.97kPa | 0.933 | 0.025 | 0.885~0.981 |
| SSM | 41.14kPa | 0.895* | 0.031 | 0.834~0.957 |
| Portal vein diameter | 14.54cm | 0.810* | 0.052 | 0.708~0.911 |
| Spleen thickness | 120.58cm | 0.915* | 0.029 | 0.859~0.972 |
| Combination | | 0.966 | 0.017 | 0.934~0.999 |

Note: Compared with combination, *$P$<0.05.

## Table 4(on next page)

Logistic regression analysis of LSM, SSM, portal vein diameter and spleen thickness with increased hepatic vein pressure

Assignment: LSM (≥27.97 kPa = 1, <27.97 kPa = 0); SSM (≥41.14 kPa = 1, < 41.14 kPa = 0); Portal vein diameter (≥ 14.54 cm = 1, < 14.54 cm = 0); Spleen thickness (≥ 120.58 cm = 1, <120.58 cm = 0).

Table 4 Logistic regression analysis of LSM, SSM, portal vein diameter and spleen thickness with increased hepatic vein pressure

| Indicator | β | SE | wald$\chi^2$ | OR | 95%CI | *P*-value |
|---|---|---|---|---|---|---|
| LSM | 0.111 | 0.068 | 2.665 | 1.117 | 0.978~1.277 | 0.103 |
| SSM | 0.131 | 0.054 | 5.885 | 1.140 | 1.025~1.267 | 0.016 |
| Portal vein diameter | 0.518 | 0.248 | 4.363 | 1.679 | 1.032~2.729 | 0.037 |
| Spleen thickness | 0.156 | 0.058 | 7.234 | 1.169 | 1.043~1.310 | 0.007 |
| Constant | -3.671 | 1.035 | 12.580 | 0.025 | 0.003~0.194 | <0.001 |

Assignment: LSM (≥27.97 kPa = 1, <27.97 kPa = 0); SSM (≥41.14 kPa = 1, < 41.14 kPa = 0); Portal vein diameter (≥ 14.54 cm = 1, < 14.54 cm = 0); Spleen thickness (≥ 120.58 cm = 1, <120.58 cm = 0).