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Doppler ultrasound compared to shear wave elastography for assessment of liver cirrhosis

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Abstract

Background The progression of liver fibrosis to cirrhosis is a dynamic process necessitating non-invasive evaluation modalities. This study aims to evaluate the ability of Doppler ultrasound studies (DUS) in defining morphological and hemodynamic blood flow changes in the hepatic vasculature coinciding with advanced liver fibrosis.

Methods A prospective study was conducted on 100 patients with liver cirrhosis (F4). All cases underwent liver stiffness (LS) measurement by shear wave elastography (SWE), along with DUS to evaluate the liver texture, splenic size, hepatic artery resistive index (HARI), portal and splenic vein diameters, portal vein velocity (PVV), and hepatic vein waveform (HVV). All measures were assessed concurrently with a highly qualified single operator.

Results Patients aged 55.5 ± 10.2 years with male predominance (72%). A highly significant correlation was found between LS by SWE and hepatic parenchymal texture, splenic size, portal vein width, and HVV (monophasic and biphasic) ($p < 0.001$). There were also high significant positive correlations ($p < 0.001$) between LS and PVV. However, there was no definitive correlation between LS and HARI, as well as splenic vein diameter.

Conclusion The widely available economic Doppler studies including portal vein velocity and hepatic vein waveform changes could be of substantial diagnostic value to liver cirrhosis.

Study design Prospective cohort study, employing descriptive and analytical statistics.

Keywords Shear wave elastography, Doppler ultrasound, Hepatic artery, Portal vein, Hepatic vein waveforms, Liver fibrosis

Background

Egypt has the highest prevalence of hepatitis C (HCV) infection globally, posing a significant public health and economic burden [1]. Despite the widely successful HCV treatment campaign, assessment of hepatic fibrosis progression is crucial in evaluating the remaining burden of HCV infection [2]. Liver fibrosis staging typically considers both the extent of fibrosis and architectural changes [3]. Liver biopsy has traditionally been the gold standard for assessing fibrosis but is costly, invasive, and associated with complications [4]. Non-invasive methods for assessing liver fibrosis have become a primary objective, leading to the development of new approaches [4].

Ultrasound is an established tool for liver assessment, and Doppler ultrasound has emerged as a non-invasive method for evaluating blood flow changes in chronic liver disease, including the detection of portal hypertension [5]. Doppler indices, such as the transformation of hepatic vein waveform from triphasic to monophasic or biphasic in cirrhotic patients with portal hypertension, have been proposed for patients with chronic hepatitis C (CHC) [6].

Elastography is a non-invasive technique commonly used for staging chronic hepatitis and has gained popularity [7]. However, its accuracy can be compromised in medium fibrosis stages (II and III) and affected by factors such as body mass index, inflammation, cholestasis,

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and steatosis [8–12]. Shear wave elastography (SWE) is a technique that monitors shear waves in the hepatic parenchyma and is considered the most important non-invasive method for liver fibrosis staging [13]. The performance of SWE demonstrated its highest efficacy when evaluating patients across different fibrosis stages. Particularly, SWE exhibited exceptional effectiveness in discerning liver fibrosis in patients classified as F0 (98.9%), F1 (97.8%), and F4 (93.3%), followed by F2 (92.8%) and F3 (90.6%). This variability in efficacy across fibrosis stages underscores the importance of considering the diagnostic accuracy of SWE in different disease progressions, thereby highlighting its potential utility as a diagnostic tool in clinical practice [14, 15].

This study aims to evaluate the role of Doppler hemodynamics of hepatic vasculature in combination with shear wave elastography in assessing liver cirrhosis and fibrosis grade F4.

Methods

A prospective cohort study was conducted from December 2021 to May 2022, involving 100 compensated liver cirrhosis patients. Ethical considerations were adhered to, and consent was obtained from patients or their families.

The study included chronic HCV-infected patients with compensated liver cirrhosis aged 18 years or older, of both genders.

Patients with congestive heart failure, post-liver transplantation, pregnancy, age below 18, and co-infection with hepatitis B virus were all excluded.

All cases were recruited to a thorough patient history.

The study included a thorough patient history, clinical examination, and laboratory tests, including full blood analysis, liver function tests, prothrombin time, activity, blood urea, and serum creatinine. Abdominal ultrasonography was performed after an 8-h fast. Doppler ultrasound was performed by an experienced operator using a GE ultrasound machine with a C5-1 curvilinear probe.

Shear wave elastography was conducted by a skilled operator using a GE machine and a C5-1 curvilinear probe. Measurements and data analysis were carried out using appropriate software and techniques.

Statistical analysis

Data analysis was conducted using IBM SPSS software (version 20.0). Descriptive statistics were used for qualitative and quantitative data. The significance of the results was determined at a 5% level using the Kruskal–Wallis test and Spearman coefficient.

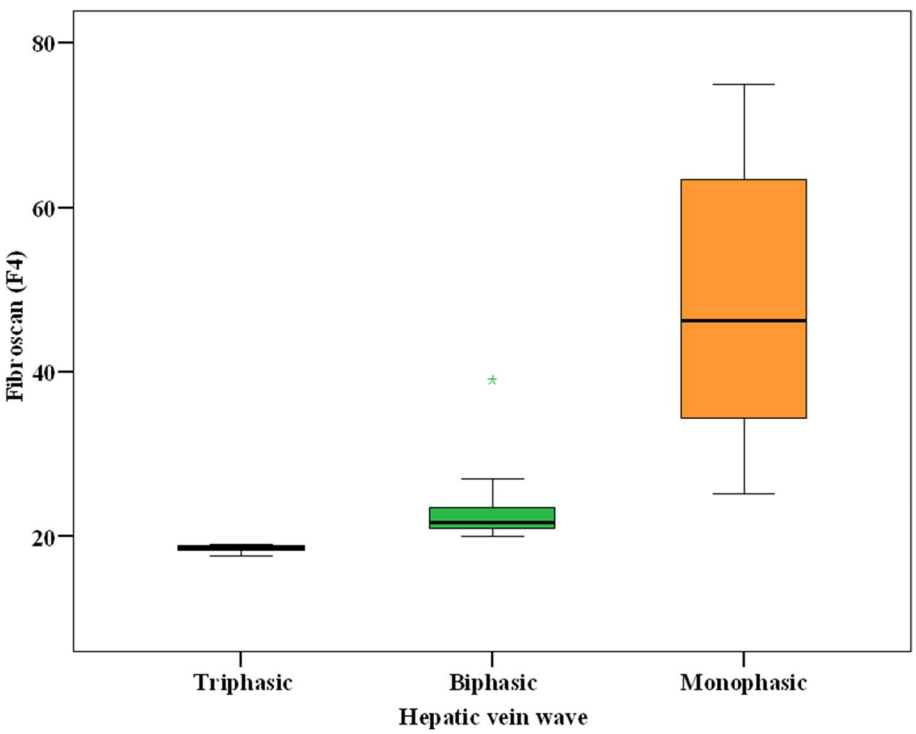

Fig. 1 Relation between hepatic vein wave and elastography (F4) ($n = 100$)

Table 1 Correlation between liver stiffness measured by elastography (F4) and different parameters

Liver stiffness (F4) vs	No	r_s	*p*
Portal vein diameter (mm)			
Normal (< 14)	**33**	0.574	< 0.001*
Enlarged (≥ 14)	**67**	0.390	0.001*
Portal vein velocity (cm/s)			
Normal (12–20)	**39**	− 0.514	0.001*
Abnormal (< 12)	**61**	− 0.701	< 0.001*
Spleen (cm)			
Normal (< 13)	**8**	0.789	0.020*
Enlarged (≥ 13)	**92**	0.499	< 0.001*
Splenic vein diameter (mm)			
Normal (< 9)	**8**	− 0.138	0.745
Enlarged (≥ 9)	**92**	0.250	0.016*
HARI			
HARI (< 75%)	**31**	0.466	0.008*
Abnormal (> 75%)	**69**	0.194	0.111

rs, Spearman coefficient; *statistically significant at $p \leq 0.05$

Results

In this prospective cohort study, 100 cirrhotic patients (72 males and 28 females) were assessed using elastography and Doppler ultrasound. Pelvi-abdominal ultrasound with hepatic Doppler and LS measurements were conducted. The mean age was 55.5 ± 10.2 years.

Regarding hepatic parenchyma, 69.0% of cases had coarse liver texture with an irregular margin, 24.0% had coarse texture with a regular margin, and 7.0% had normal liver parenchyma. The mean splenic size was 17.58 ± 2.69 cm, and 92% of patients had an enlarged spleen. The mean splenic vein diameter was 14.96 ± 3.06 mm, and it was dilated in 92% of patients. The mean portal vein diameter was 16.44 ± 1.53 mm, and 67.0% of patients had an enlarged portal vein diameter. The mean portal vein velocity was 9.26 ± 1.45 cm/s, and 61.0% of patients had decreased portal vein velocity below the normal range.

Hepatic vein waveforms were observed as triphasic in 7.0% of patients, biphasic in 24.0%, and monophasic in 69.0% (Fig. 1). The mean value of normal HARI (less than 75%) was 0.67 ± 0.07, seen in 30% of cases, while

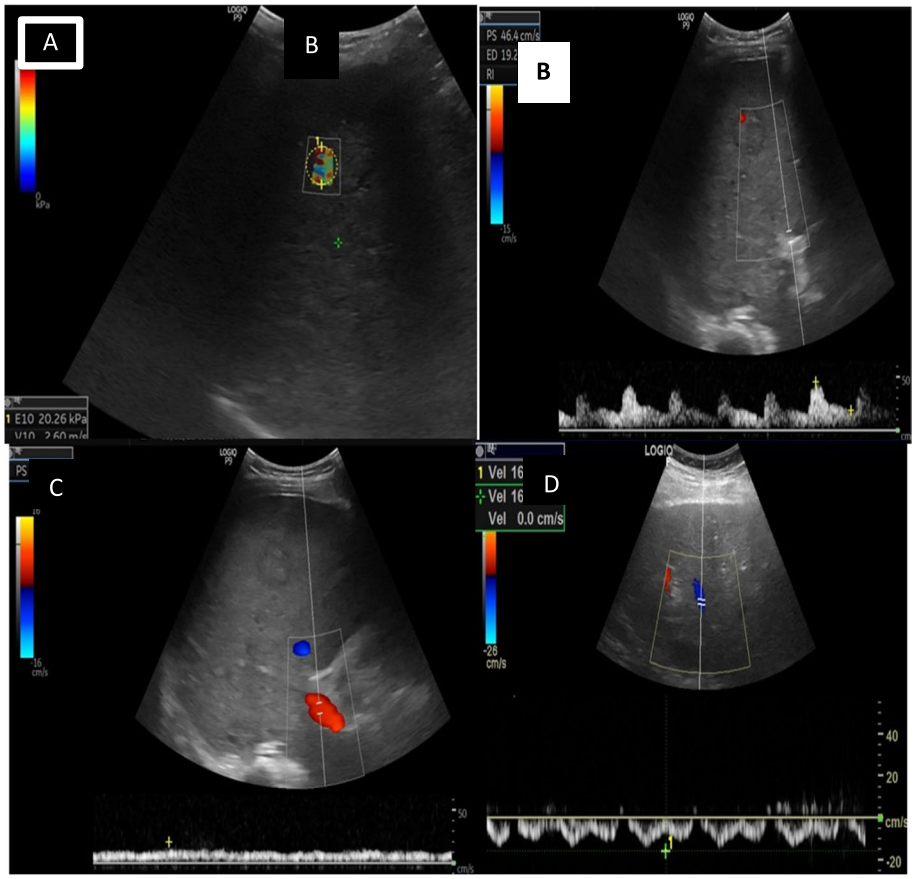

Fig. 2 A 65-year-old male patient with liver cirrhosis shows **A** liver elasticity measurement with elastography = 20.2 kPa (F4), **B** portal vein velocity = 20 cm/s, **C** HARI = 0.59, and **D** hepatic vein flow is biphasic with velocity = 16 cm/s

abnormal HARI (more than 75%) had a mean value of 0.84 ± 0.06, observed in 70.0% of patients. The mean value of liver stiffness measured by shear wave elastography (F4) was 39.72 ± 18.05 kPa, ranging from 17.60 to 75.0 kPa (Table 1) (Figs. 2, 3, 4, 5, and 6).

Significant correlations were found between LS (F4) and hepatic parenchymal texture, portal vein velocity, portal vein diameter, and hepatic vein waveforms. However, there was no significant correlation between LS (F4) and HARI or splenic vein diameter (Tables 1 and 2) (Figs. 1, 2, 3, 4, 5, and 6).

Discussion

Screening and monitoring acute and chronic liver diseases through non-invasive methods is an ongoing challenge to reduce the reliance on biopsy protocols and to better assess the progression of liver disease. Our study highlights the significance of Doppler ultrasound as a valuable tool in evaluating liver cirrhosis occurrence [16].

The diagnosis and staging of liver fibrosis have seen advancements with the use of shear wave elastography, a non-invasive technique that allows for repeated measurements in patients with advanced chronic liver diseases [17].

Doppler ultrasound plays a crucial role in evaluating hemodynamic changes within cirrhotic livers, encompassing both morphological and hemodynamic aspects of the portal vein, hepatic veins, and hepatic vasculature [16, 18].

Our study involved 100 patients, consisting of 72 males and 28 females, with an average age of 55.5 ± 10.2 years. In our study, the mean splenic size was 17.58 ± 2.69 cm, and 92% of patients exhibited an enlarged spleen. Similarly, the mean splenic vein diameter was 14.96 ± 3.06 mm, with 92% of patients having dilation beyond typical levels. Additionally, the mean portal vein diameter was 16.44 ± 1.53 mm, and an enlarged portal vein was observed in 67.0% of cases. Portal vein velocity showed a mean value of 9.26 ± 1.45 cm/s, with 61.0% of patients having decreased portal vein velocity below normal levels (Figs. 3 and 6). These findings align with Kayacetin et al. [19, 20], who reported larger portal and splenic vein diameters in liver cirrhosis and noted reduced portal vein velocity in cirrhotic patients.

Changes in hepatic flow are associated with abnormal intrahepatic shunt vessels, which contribute to alterations

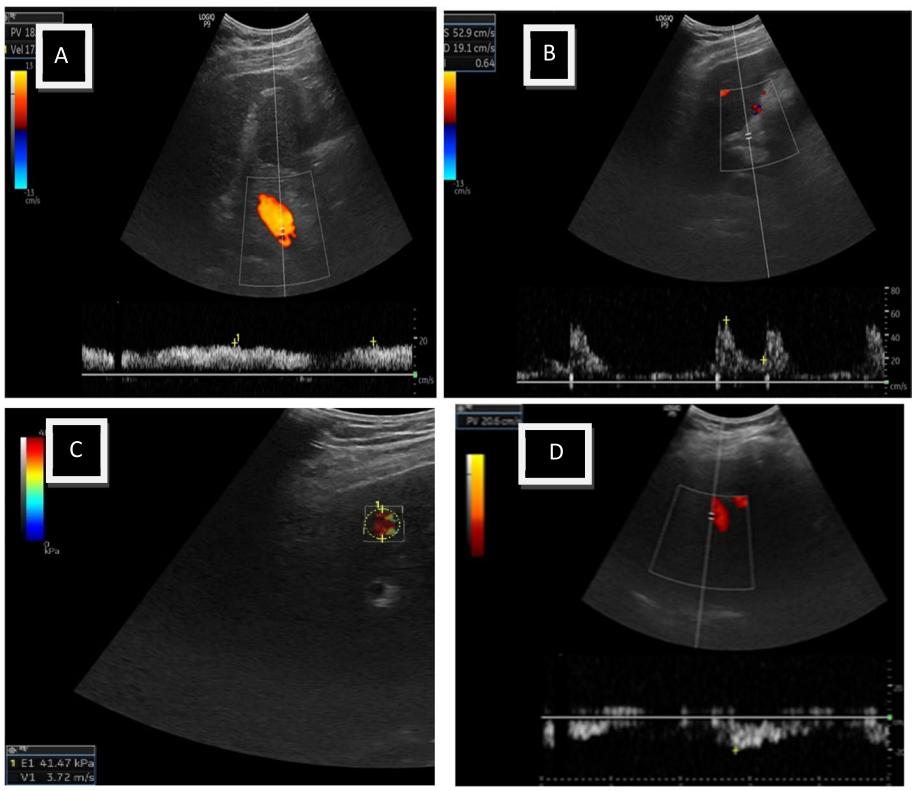

Fig. 3 A 54-year-old male patient with liver cirrhosis shows **A** liver elasticity measurement with elastography = 31.9 kPa (F4), **B** portal vein velocity = 9.5 cm/s, **C** HARI = 0.79, and **D** hepatic vein flow is biphasic with velocity = 31 cm/s

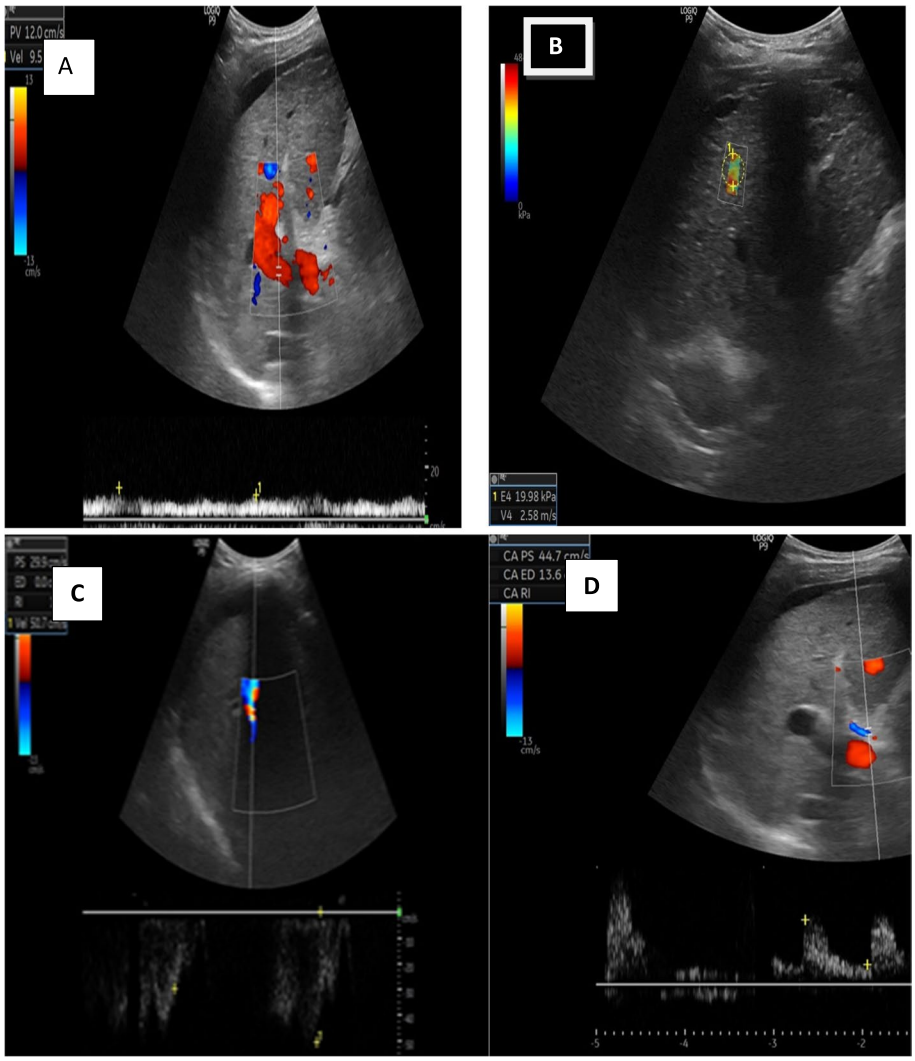

Fig. 4 Male patient 76 years with liver cirrhosis shows **A** liver elasticity measurement with elastography = 26.3kps (F4), **B** portal vein velocity = 20.6 cm/s, **C** hepatic vein flow is monophasic mainly with velocity = 25 cm/s, and **D** HARI = 0.51

in hepatic venous waveforms. In the current study, 7.0% of patients had triphasic hepatic vein waveforms, 24.0% had biphasic waveforms, and 69.0% had monophasic waveforms. These results are consistent with Sudhamshu et al. [21], who concluded that changes in cirrhotic livers are primarily due to hepatic hemodynamic alterations.

The hepatic architectural deterioration seen in patients with chronic hepatic disease leads to circulatory changes, particularly in the hepatic arteries [21]. In the current study, the mean value of abnormal hepatic artery resistive index (HARI) (greater than 75%) was 0.84 ± 0.06, while normal HARI (below 75%) was 0.67 ± 0.07. High HARI values were associated with liver cirrhosis, in line with findings by Salvatore et al. [22], who observed rising HARI levels in hepatic patients with hepatitis C. Similarly, Piscaglia et al. [23] found higher HARI levels in patients with marked liver fibrosis, as hepatic artery resistance indices appear to be influenced by hepatic inflammation and fibrous tissue deposition within the liver parenchyma.

The current study underscores the importance of Doppler ultrasound parameters in the grading of hepatic fibrosis. We found a highly significant correlation ($p < 0.001$) between liver stiffness (F4) measured by elastography and portal vein velocity, consistent with Elwan et al. [24], who documented a significant correlation between liver fibrosis degree and portal vein velocity. This correlation may be attributed to hepatic fibrosis leading to increased parenchymal resistance [24].

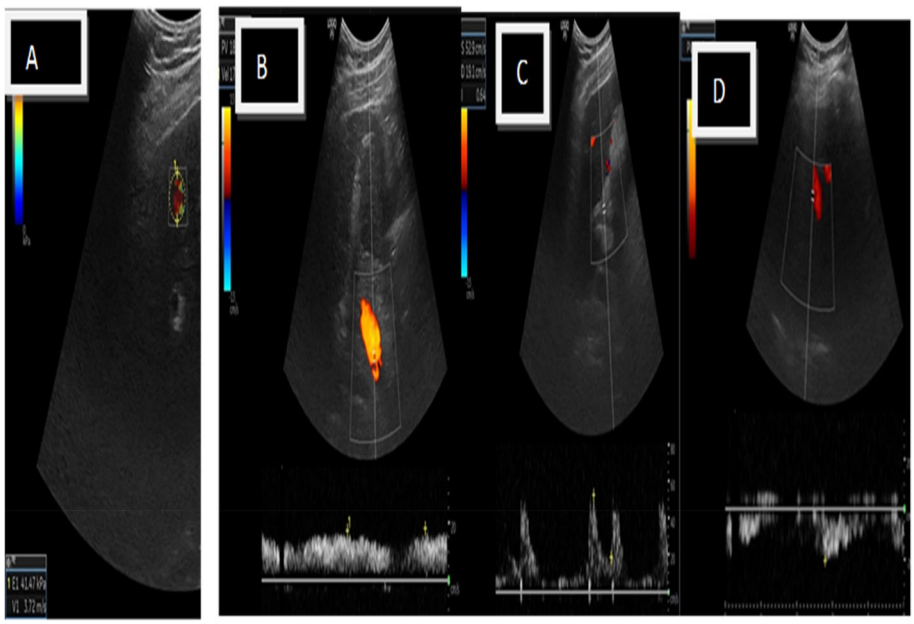

Fig. 5 A 55-year-old female patient with liver cirrhosis shows **A** liver elasticity measurement with elastography = 41 kPa (F4), **B** portal vein velocity = 18 cm/s, **C** HARI = 0.64, and **D** hepatic vein flow is monophasic with velocity = 20.6 cm/s

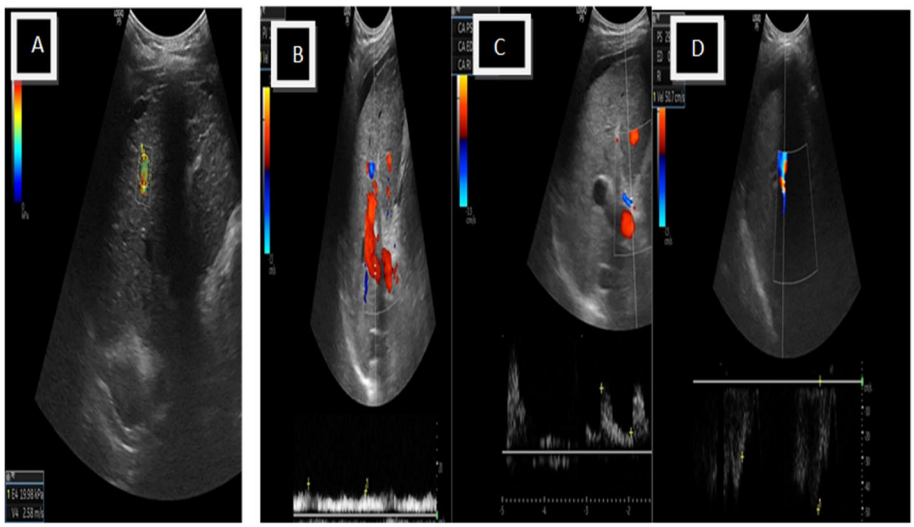

Fig. 6 A 44-year-old female patient with liver cirrhosis shows **A** liver elasticity measurement with elastography = 19.9 kPa (F4), **B** portal vein velocity = 9.5 cm/s, **C** HARI = 0.70, and **D** hepatic vein flow is biphasic with velocity = 50 cm/s

However, no significant correlation was found between HARI and liver stiffness (F4) results (Table 1). This is in line with Lim et al. [25], who did not observe a relationship between HARI values and liver stiffness. Hanafi et al. [26] and Elwan et al. [24] also noted no significant differences in HARI results between patients with mild to moderate fibrosis and those with marked fibrosis, although Lutz et al. [18] found significantly higher HARI values in cirrhosis.

Furthermore, our study identified a correlation between liver stiffness (F4) and hepatic vein waveforms, specifically monophasic and biphasic waveforms, with a P value < 0.001 (Figs. 3 and 6) (Table 2). However, no correlation was observed with triphasic waveforms. El Shaer et al. [27] documented that hepatic vein waveforms exhibited a strong correlation with the severity of liver cirrhosis. Additionally, a high correlation ($P < 0.001$) was found between liver stiffness and the middle of hepatic

Table 2 Relation between hepatic vein wave and liver stiffness measured by elastography (F4) ($n=100$)

	Hepatic vein wave			*H*	*p*
	Triphasic ($n=7$)	Biphasic ($n=24$)	Monophasic ($n=69$)		
Elastography (F4)					
Mean ± SD	18.53 ± 0.54	22.91 ± 3.91	47.72 ± 16.07	61.364*	< 0.001*
Median (Min.–Max.)	18.60 (17.60–19.0)	21.65 (20.0–39.0)	46.20 (25.10–75.0)		
Sig. bet. grps	$p_1=0.174$, $p_2<0.001^*$, $p_3<0.001^*$				

SD, standard deviation; *H*, *H* for Kruskal–Wallis test; pairwise comparison between each 2 groups was done using post hoc test (Dunn's for multiple comparisons test); *p*, *p* value for comparing between different categories; p_1, *p* value for comparing between triphasic and biphasic; p_2, *p* value for comparing between triphasic and monophasic; p_3, *p* value for comparing between biphasic and monophasic; *Statistically significant at $p \leq 0.05$

vein waveforms. Lutz et al. [18] concluded that right hepatic vein Doppler ultrasound is a promising method for liver disease staging and could potentially reduce the need for biopsies, especially in cases of high-stage fibrosis and cirrhosis, although no significant correlation was noted in low-grade fibrosis [18].

Limitations

Our study has certain limitations, including a small sample size and grading of fibrosis using shear wave elastography by a single radiologist. Consequently, interobserver variations could not be assessed. Additionally, false-positive, or false-negative results in Doppler ultrasound could be influenced by the stage of respiration and cardiac reflux. Moreover, it is only applicable to cases with advanced fibrosis or cirrhosis, and further research is still needed for evaluating its efficacy in earlier stages of fibrosis.

Conclusions

In conclusion, this study highlights the substantial role of hepatic Doppler hemodynamic changes, in defining advanced liver fibrosis. Accordingly, the easily performed, widely available, and inexpensive Doppler ultrasonic studies can provide insights into alterations in intrahepatic vascular resistance, thereby increasing the accuracy of detecting liver cirrhosis.

Abbreviations

HARI	Hepatic artery resistive index
HCV	Hepatitis C virus
CHC	Chronic hepatitis
HV	Hepatic vein
HVRI	Hepatic vein resistive index
US	Ultrasound
SWE	Shear wave elastography
kPa	Kilopascals
ROI	Region of interest
LS	Liver stiffness
PVV	Portal vein velocity

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Not applicable.

Authors' contributions

Conceptualization and data curation: SAA and HSE. Formal analysis: HSE, MSA, and SAA. Investigation: SAA. Methodology: MSA project administration and resources: MSA. Software: HSE. Supervision: MSA. Validation and visualization: HSE. Writing the original draft; HSE. Writing review—revision and editing: HSE, MSA, and SAA.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional Review Board (IRB) IRB Number (00419/2022) of National Liver Institute Menoufia University and with the Helsinki Declaration of 1964 and later versions. The committee's reference number is unavailable (NOT applicable). Consent was obtained from the patients since it was a retrospective study.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The authors declare that they have no competing interests.

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