

## To study doppler and triphasic CT findings in patients of NASH induced cirrhosis diagnosed on transient elastography

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### ABSTRACT

**Introduction:** Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly NAFLD, includes a spectrum from simple steatosis to non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis. Given the invasiveness of liver biopsy, noninvasive tools such as transient elastography (TE), Doppler ultrasound, and triphasic CT have emerged as alternatives for staging liver fibrosis. This study aimed to assess Doppler and CT findings in NASH-induced cirrhosis patients diagnosed on TE.

**Materials and Methods:** This observational study included 51 patients (age >18 years) with NASH-related cirrhosis and liver stiffness >13 kPa on Fibroscan®. Exclusion criteria included viral hepatitis, alcohol use, and renal insufficiency. All participants underwent Doppler ultrasound and triphasic CT scans. Parameters such as hepatic artery resistive index (HARI), portal vein velocity, hepatic vein phasicity, caudate-right lobe ratio (CRL), and liver-to-spleen attenuation ratio were recorded. Statistical analyses were performed using SPSS v23.

**Results:** Most patients (68.6%) were in the F4 fibrosis stage. A strong positive correlation was observed between Fibroscan and portal vein diameter, while HARI and portal vein velocity were negatively correlated. HARI <0.77 showed 97.1% sensitivity and 90% accuracy in predicting F4 fibrosis. Triphasic hepatic vein waveform decreased with advanced fibrosis. Liver-to-spleen attenuation <0.8 correlated with higher liver stiffness, while CRL >0.65 was seen in advanced fibrosis.

**Conclusion:** Doppler and CT parameters, especially HARI and portal vein velocity, significantly correlate with Fibroscan scores, enhancing noninvasive diagnosis of advanced NASH-related fibrosis.

**Keywords:** NASH, Doppler ultrasound, Transient elastography, Fibroscan, Cirrhosis, Triphasic CT

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## 1. INTRODUCTION

Metabolic dysfunction-associated liver disease (MASLD), formerly known as NAFLD, is characterized by fat accumulation in over 5% of liver cells without alcohol or drug-related causes. It includes a range of liver conditions such as NAFL, NASH, fibrosis, and cirrhosis.<sup>1</sup> Globally, MASLD affects around 25% of the population, with NASH being most prevalent in the Middle East and South America and projected to become the leading cause of chronic liver disease and liver transplantation.<sup>2,3</sup> In India, adult NAFLD prevalence ranges from 6.7% to 55.1% and is a significant contributor to unexplained liver enzyme elevation and cryptogenic cirrhosis.<sup>4</sup>

Chronic progressive liver diseases, notably NAFLD, frequently lead to liver fibrosis and are closely associated with obesity, insulin resistance, and metabolic disorders like diabetes and atherosclerosis.<sup>5</sup> Fibrosis can also arise from chronic infections (hepatitis, HIV) or exposure to drugs and toxins, and is driven by oxidative stress, extracellular matrix accumulation, and activation of hepatic stellate cells via mediators such as PDGF, TNF- $\alpha$ , TGF- $\beta$ , and reactive oxygen species, ultimately

resulting in irreversible liver damage.<sup>6</sup>

Liver biopsy is still considered the gold standard for evaluating liver damage and diagnosing NAFLD, including its progression to NASH, by detecting fat accumulation, inflammation, and fibrosis.<sup>7</sup> However, due to its invasive nature, limited sampling, and observer variability, there has been a growing shift toward noninvasive methods.<sup>8</sup> Among these, elastography has emerged over the past two decades as a leading technique, using ultrasound or MRI to assess liver tissue stiffness through shear wave analysis, providing a reliable and safer alternative for diagnosing and staging liver fibrosis.<sup>9</sup>

Transient elastography (TE; FibroScan®) and Doppler ultrasound are widely used noninvasive techniques for evaluating liver disease. TE is a key tool for staging liver fibrosis in both acute and chronic conditions, though its accuracy may be reduced in moderate fibrosis and influenced by factors such as inflammation, BMI, steatosis, and cholestasis. Doppler ultrasound, on the other hand, is valuable for assessing hepatic blood flow, with the hepatic artery resistive index (HARI) serving as an important parameter for monitoring microcirculatory resistance in various liver conditions, including fatty liver, alcoholic liver disease, chronic hepatitis, and post-transplant patients.<sup>10</sup>

CT assesses hepatic steatosis by measuring liver attenuation values in Hounsfield units (HU), which decrease as fat content increases. While unenhanced CT provides better accuracy than contrast-enhanced scans—especially when using liver-to-spleen attenuation difference (CTL-S) to avoid inter-scanner variability—CT is limited in detecting mild steatosis and involves radiation exposure, making it less suitable for routine NAFLD evaluation, though useful in specific cases like living liver donor assessment. Thus, the aim of the study was to study Doppler ultrasound and Triphasic CT findings in patients of NASH induced cirrhosis diagnosed on Transient Elastography.

## 2. MATERIALS AND METHODS

The hospital-based observational study was conducted from January 2020 to September 2021 at a tertiary care teaching hospital in Himachal Pradesh, North India, involving the Departments of Radiology and Gastroenterology & Hepatology. The study population included adult patients (above 18 years) diagnosed with liver cirrhosis who presented to the Radiology department. A total of 51 patients with NASH-related cirrhosis and liver stiffness measurement (LSM) values exceeding 13 kPa on transient elastography were enrolled. Subjects were included after meeting the specified inclusion and exclusion criteria and providing informed consent. Detailed clinical history and examination findings were recorded on a structured proforma. Patients with renal insufficiency, jaundice, ascites, chronic alcohol intake, hepatitis B or C infection, congestive cardiac failure, pregnancy, or a history of adverse reactions to iodinated contrast agents were excluded from the study.

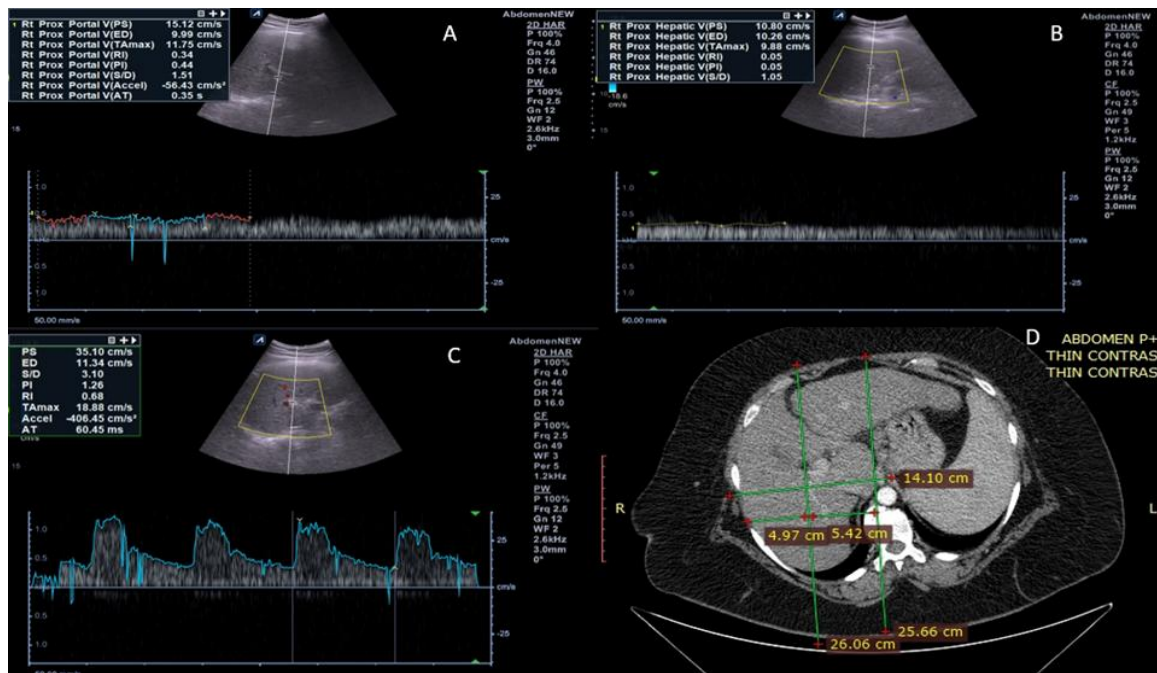
Following a general physical examination and obtaining written informed consent, contrast-enhanced CT (CECT) of the abdomen was performed using a 16-slice MDCT scanner (Brilliance 16, Philips). A non-ionic contrast medium with 300 mg/ml iodine concentration was administered intravenously according to the patient's weight using an 18G cannula through an antecubital or accessible vein at a rate of 3.5–4.5 ml/s with a pressure injector (Medrad-Vistron CT Injection System). Scanning parameters included a supine position with arms raised, slice thickness of 0.5 mm, reconstruction interval of 0.8 mm, pitch of 1.25, and 1 mm increment. Image interpretation was carried out on a dedicated workstation using post-processing techniques like maximum intensity projection (MIP), multiplanar reformation (MPR), and volume rendering (VR). Two radiologists independently analyzed all images, followed by a joint session to reach consensus on any discrepancies.

Liver stiffness was assessed using transient elastography (TE) with the FibroScan device (Echosens Touch 502), applying low-frequency (50 Hz) vibrations and measuring shear wave propagation through liver tissue using pulse-echo ultrasound. The liver stiffness values ranged from 2.5 to 75 kPa, with higher values indicating greater stiffness and lower elasticity.

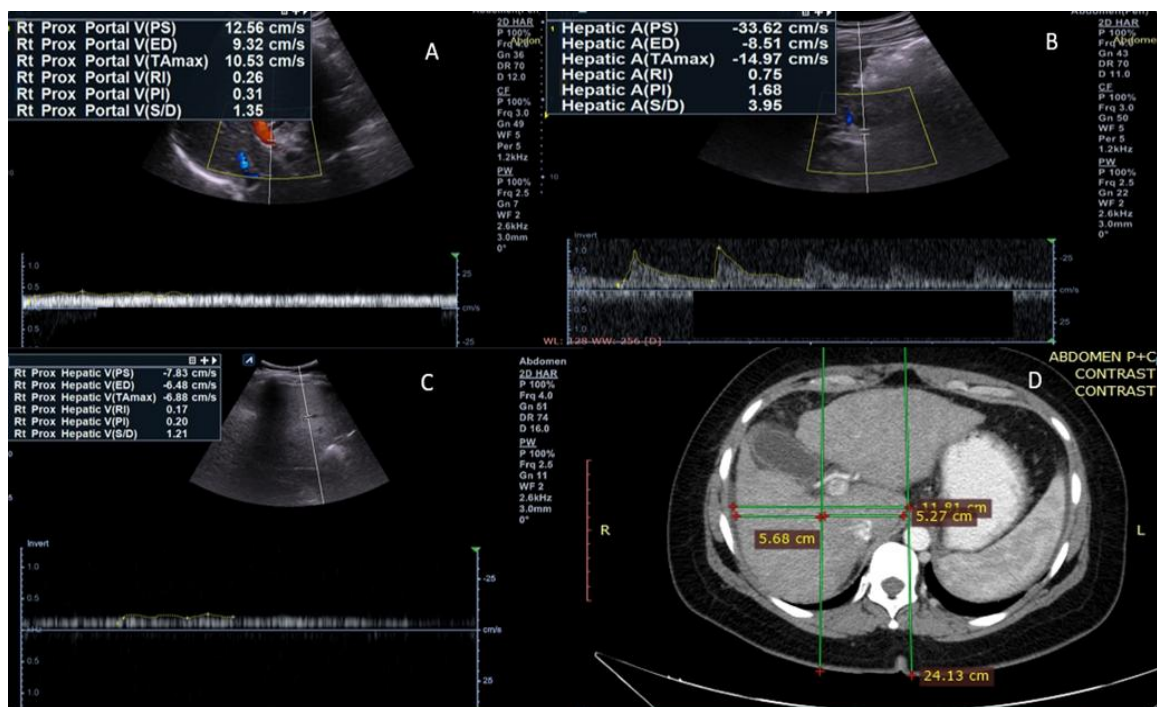
Doppler ultrasound was performed with the patient in a supine position using the Alpinion E-CUBE 8 Diamond system equipped with a 3–5 MHz convex transducer. Patients were instructed to hold their breath briefly after deep inspiration during measurements. Liver span was measured, and the middle hepatic vein and proper hepatic artery were assessed via the right costal margin. Angle correction was applied where necessary, and the hepatic artery resistive index (RI) was automatically calculated as the ratio of end-diastolic to peak systolic velocity, based on a manually selected cardiac cycle. All Doppler findings were independently analyzed by two radiologists at different times, followed by a consensus reading to resolve any discrepancies.

## 3. STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analyzed using IBM SPSS version 23. Quantitative variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Unpaired t-test was used for comparing quantitative variables, and chi-square or Fisher's exact test for categorical variables. A 95% confidence interval was applied, with  $p \leq 0.05$  considered statistically significant. Results were presented in tables and graphs with brief descriptions.

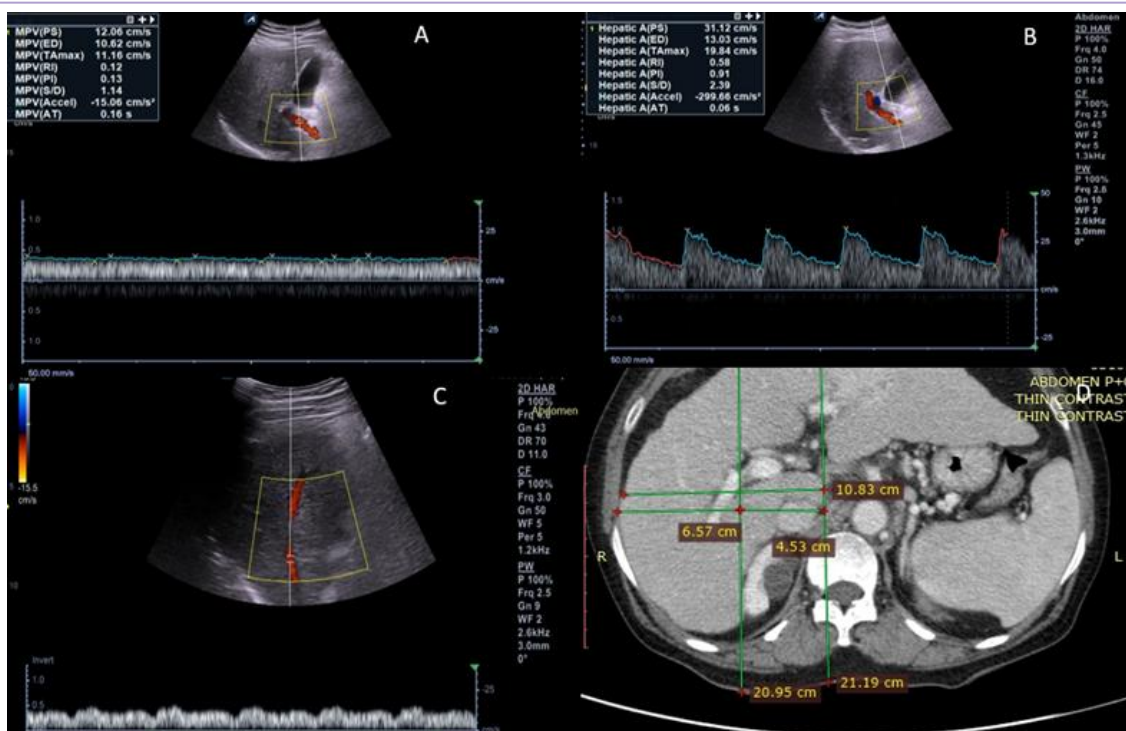


**Case 1:** 62 years old female with type 2 diabetes mellitus and fibroscan LSM value of 43.9kPa. A) Portal vein doppler shows reduced portal vein velocity of 15.12 cm/s. B) Hepatic vein doppler shows a monophasic waveform. C) Hepatic arterial doppler shows markedly reduced RI of 0.68. D) Triphasic CECT abdomen in the same patient in venous phase shows nodular liver outline with CRL of 1.10

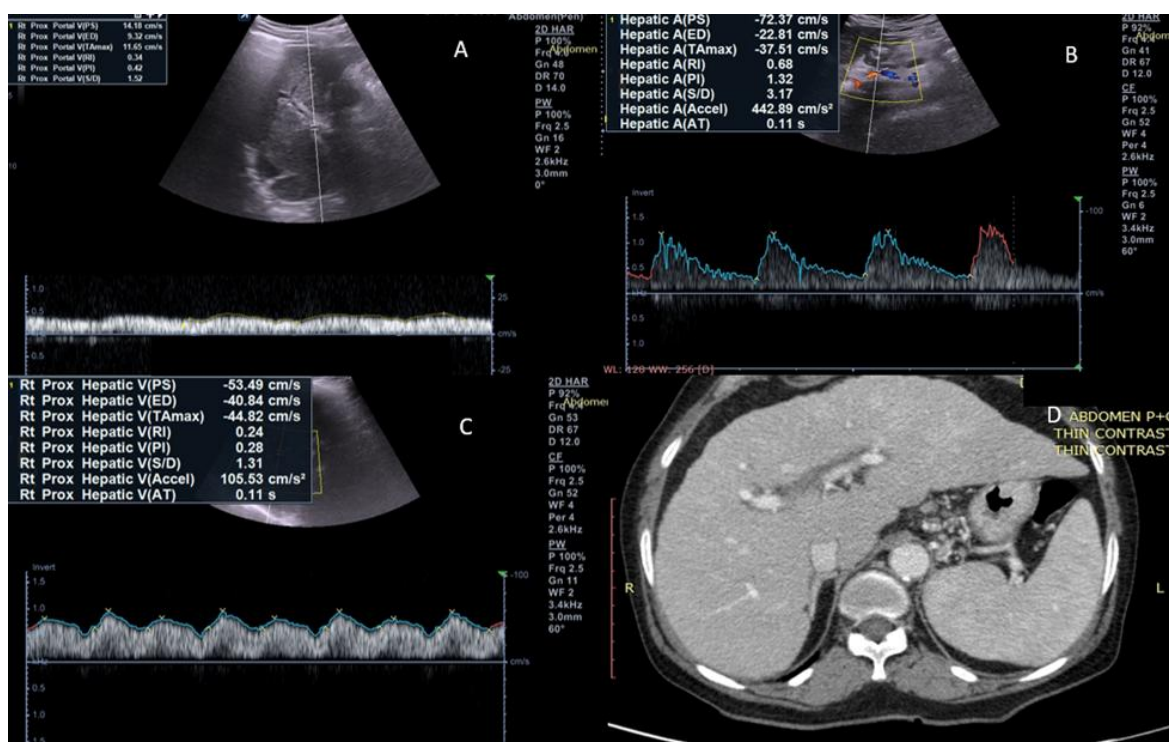


**CASE 2:** 35 year old male with type 2 diabetes mellitus and hypertension with LSM values of 43.5kPa. A) Portal vein doppler shows reduced PSV of 12.5 cm/s. B) Hepatic arterial doppler shows marginally reduced RI of 0.75. C) Hepatic vein doppler in the same patient shows monophasic waveform. D) Triphasic CECT abdomen shows nodular liver outline with CRL value of 0.92





**CASE 3:** 50 year old male with history of chronic steroid intake and LSM value of 34kPa. A) Portal vein doppler reveals reduced PSV of 12.06 cm/s. B) Hepatic arterial doppler in the same patient reveals reduced RI of 0.58. C) Hepatic venous doppler reveals monophasic waveform. D) Triphasic CECT abdomen in same patient in its venous phase shows nodular liver outline with CRL of 0.70.



**CASE 4:** 67 year old male with fibroscan LSM values of 41kPa. A) Portal vein doppler shows reduced PSV of 14.18cm/s. B) Hepatic arterial doppler shows reduced RI of 0.68. C) Hepatic venous doppler in the same patient shows monophasic waveform. D) Triphasic CECT abdomen in this patient shows nodular liver outline with CRL value of 0.98.

#### 4. RESULTS

**Table.1: Demographic, Clinical, and Imaging Characteristics of Study Participants (n=51)**

Parameter	Frequency	Percentage
Age (in years)		
20-40	4	7.8%
40-60	41	80.4%
Above 60	6	11.8%
Gender		
Male	23	46%
Female	27	54%
Comorbidities		
NO	28	54.9%
YES	23	45.1%
Various Comorbidities		
Chronic Steriod Intake	2	3.9%
DM2	13	25.5%
DM2,HTN	3	5.9%
DM2, Hyperlipidemia	1	2.0%
HTN	1	2.0%
HTN, DM2	1	2.0%
Hyperlipidemia	1	2.0%
No Comorbidity	29	56.9%
Fibroscan classification of Fibrosis (in Kpa)		
F3 (Severe Liver Scarring)	16	31.4%
F4 (Advanced Liver Scarring)	35	68.6%
Portal Vein Velocity (cm/s)		
Less than 15	30	58.8%
More than 15	21	41.2%
HARI (Hepatic Artery Resistive Index)		
Less than 0.77	38	74.5%
More than 0.77	13	25.5%
Phasicity of Hepatic Vein		
Biphasic	8	15.7%
Monophasic	18	35.3%
Triphasic	25	49.05%

Table.1 summarizes the demographic, clinical, and imaging profiles of 51 patients included in the study. Most participants were aged 40–60 years (80.4%), with a slightly higher proportion of females (54%) than males (46%). About 45.1% had comorbidities, the most common being type 2 diabetes mellitus (25.5%). According to Fibroscan, the majority had advanced liver scarring (F4, 68.6%), while 31.4% had severe scarring (F3). Doppler ultrasound parameters revealed that 58.8% had portal vein velocities below 15 cm/s, and 74.5% had a hepatic artery resistive index (HARI) below 0.77.

Regarding hepatic vein phasicity, 49.05% showed triphasic, 35.3% monophasic, and 15.7% biphasic waveforms, indicating varying degrees of liver hemodynamic alterations among the patients.

**Table.2: Correlation of Fibroscan Values with Doppler Ultrasound Parameters in Patients with Liver Fibrosis**

Parameter	Fibroscan	
	Pearsson Correlation	p-value
Portal Vein Diameter	0.884	<0.001
MPVV	-0.875	<0.001
HARI (Hepatic Artery Resistive Index)	-0.949	<0.001
CRL	0.164	0.251

Table.2 demonstrates the strength and significance of correlations between Fibroscan (liver stiffness) values and various Doppler ultrasound parameters. Liver stiffness showed a strong positive correlation with portal vein diameter ( $r = 0.884$ ,  $p < 0.001$ ), indicating that larger portal vein diameters were associated with higher Fibroscan values. Mean portal vein velocity (MPVV) and hepatic artery resistive index (HARI) exhibited strong negative correlations with Fibroscan values ( $r = -0.875$  and  $-0.949$ , respectively,  $p < 0.001$ ), suggesting that lower MPVV and HARI were associated with increased liver stiffness. In contrast, the caudate-to-right lobe ratio (CRL) showed no significant correlation ( $r = 0.164$ ,  $p = 0.251$ ), indicating it was not a reliable predictor of liver stiffness in this study.

**Table.3: Diagnostic Performance of Fibroscan (F4) Combined with Doppler Ultrasound Parameters in Detecting Advanced Liver Fibrosis**

	Sensitivity	Specificity	Positive Predictive value	Negative Predictive Value	Accuracy	Positive Likelihood ratio	Negative Likelihood ratio
Fibroscan (F4) and monophasic hepatic vein waveform	45.7%	87.5%	88.9%	42.4%	58.8%	3.66%	0.620%
Fibroscan(F4) and Hepatic artery resistive index(< 0.77)	97.1%	75%	89.5%	92.3%	90%	3.89%	0.038%
Fibroscan(F4) in Mean Portal Vein Velocity	80%	94%	93%	76%	90.2%	2.94%	0.143%

Table.3 shows the diagnostic accuracy of Fibroscan (F4) when combined with different Doppler ultrasound parameters for detecting advanced liver fibrosis. Combining Fibroscan with a monophasic hepatic vein waveform showed moderate specificity (87.5%) but low sensitivity (45.7%), resulting in a modest overall accuracy of 58.8%. Using Fibroscan alongside hepatic artery resistive index (HARI < 0.77) greatly improved sensitivity to 97.1% and achieved 90% accuracy, indicating strong ability to correctly identify patients with advanced fibrosis. Fibroscan combined with mean portal vein velocity demonstrated high specificity (94%) and good sensitivity (80%), yielding the highest overall accuracy of 90.2% among the three combinations. These findings suggest that integrating Fibroscan with Doppler parameters, particularly HARI or portal vein velocity, enhances the noninvasive detection of advanced liver fibrosis.

**Table.4: Cross-tabulation of Fibroscan Values and Liver-to-Spleen (L/S) Attenuation Ratio**

Cross tabulation Between Fibroscan and L/S attenuation			
	Liver to Spleen Attenuation		Total
	<0.8	>0.8	
Fibroscan			
<20	15	1	16
>20	1	34	35
Total	16	35	51

Table.4 shows the relationship between liver stiffness measured by Fibroscan and hepatic fat content assessed using the L/S attenuation ratio on CT. Among patients with Fibroscan <20 kPa, 15 had L/S ratio <0.8, indicating significant steatosis, while only 1 had L/S >0.8. In the Fibroscan >20 kPa group, 34 patients had L/S <0.8 and 1 had L/S >0.8, suggesting that higher liver stiffness is strongly associated with lower L/S ratio, reflecting greater hepatic fat deposition and fibrosis.

**Table.5: Comparison of Fibroscan Values by CRL Categories**

	CRL	N	Mean	Std. Deviation
Fibroscan	< 0.65	12	17.4000	6.16382
	>0.65	9	30.3128	10.20230

Table.5 compares Fibroscan liver stiffness measurements based on CRL values. Patients with CRL <0.65 had a mean Fibroscan value of 17.4 kPa, while those with CRL >0.65 had a higher mean value of 30.31 kPa, indicating that increased CRL is associated with greater liver stiffness and more advanced fibrosis. An independent samples t-test revealed a significant correlation ( $p < 0.005$ ), indicating that increased liver stiffness is associated with higher CRL, with most patients having CRL >0.65 as Fibroscan values rise.

## 5. DISCUSSION

Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver disease in the United States and is increasingly prevalent in developing countries, including India. NAFLD includes two main subtypes: the relatively benign NAFL and the progressive NASH, which can lead to fibrosis and cirrhosis. While liver biopsy is the gold standard for diagnosis and staging, its invasiveness and sampling limitations have prompted the development of noninvasive methods such as transient elastography, with the Fibroscan 502 improving accuracy by automatically selecting the appropriate probe based on skin-to-liver distance.

In our study of 51 patients, the majority were aged 40–50 years (58%), followed by those above 60 years (20%), with the least representation from the 20–40 age group (8%), indicating the common onset of NAFLD and NASH in middle age. These findings are in agreement with studies by Nomura H et al.<sup>12</sup> and Lonardo A et al.,<sup>13</sup> which also observed a higher prevalence of NASH in individuals aged 40–49 years. Gender distribution showed a slight female predominance (54%), similar to results from Summart U et al.<sup>14</sup> and Suzuki A et al.,<sup>15</sup> who noted a greater incidence of NAFLD in women, especially in the postmenopausal age group. This pattern may be linked to declining estrogen levels with age, resulting in increased visceral adiposity, hyperlipidemia, and insulin resistance. These metabolic changes elevate the risk for type 2 diabetes and NAFLD. Hence, age-related hormonal shifts appear to significantly influence NAFLD susceptibility, particularly among women.

NAFLD is a growing global concern, with most deaths attributed to cancers and cardiovascular disease rather than liver failure, and is closely linked to metabolic syndrome and type 2 diabetes. In our study, despite this association, 56.9% had no comorbidities, indicating that unknown genetic or environmental factors may also contribute to its progression. All

included patients in our study had Fibroscan values above 13 kPa and were categorized into F3 (13–20 kPa) and F4 (>20 kPa), indicating severe and advanced liver scarring, respectively. A majority (68.6%) were in the F4 stage, with a mean Fibroscan value of 27.2 kPa and a maximum of 55.9 kPa. Notably, these thresholds differed slightly from those used in previous studies,<sup>8,16</sup> highlighting variability in fibrosis staging approaches.

Our study demonstrated a significant positive correlation between portal vein diameter and Fibroscan values ( $p < 0.001$ ), suggesting that as liver fibrosis advances, portal hypertension develops, leading to an increase in portal vein diameter. In contrast, a significant negative correlation was observed between portal vein velocity and Fibroscan scores ( $p < 0.001$ ), indicating reduced portal vein flow with increasing fibrosis severity. These findings are consistent with those of EM Elshaer,<sup>17</sup> who also reported a significant correlation between Fibroscan results and portal vein diameter, and with studies by Erdogmus B et. al<sup>18</sup> and Iwao T et. al,<sup>19</sup> which noted declining portal vein velocity in cirrhotic and fibrotic patients. In our analysis, a mean portal vein velocity (MPVV) of less than 15 cm/s showed 80% sensitivity and 94% specificity for predicting F4-stage NASH, with positive and negative predictive values of 93% and 76%, respectively. This reinforces the utility of portal vein measurements as non-invasive indicators of advanced liver fibrosis.

In our study, HARI also showed a significant negative correlation with Fibroscan values ( $p < 0.001$ ), with higher fibrosis associated with lower HARI, likely due to compensatory hepatic artery dilation from reduced portal vein flow. These results align with previous studies by Sabry M et al.,<sup>20</sup> confirming that advanced fibrosis in NASH markedly lowers HARI. A HARI below 0.77 predicted F4 fibrosis with 97.1% sensitivity, 75% specificity, and positive and negative predictive values of 89.5% and 92.3%, respectively.

In our study, triphasic waveform was most common overall, but monophasic waveform predominated with higher Fibroscan values, likely due to hepatocyte swelling from fatty infiltration. This aligns with previous studies<sup>21,22</sup> showing monophasic waveforms increase with NAFLD/NASH severity. For F4 Fibroscan, sensitivity was 45.7%, specificity 87.5%, with positive and negative predictive values of 88.5% and 42.4%, respectively.

In our study, most patients with higher Fibroscan scores had CRL values  $> 0.65$ , indicating advanced liver scarring, though no linear correlation was observed, suggesting CRL changes occur mainly in advanced cirrhosis. Similar findings were reported by Bolog N et. al<sup>23</sup> and Awaya H et. al,<sup>24</sup> confirming that elevated CRL reflects severe fibrosis. Liver-to-spleen (L/S) attenuation was  $< 0.8$  in most patients with Fibroscan  $< 20$  kPa, indicating early steatosis, while in those with Fibroscan  $> 20$  kPa, L/S attenuation was  $> 0.8$ , reflecting progression to fibrosis and reduced fat content. These results align with previous studies<sup>25,26,27</sup> highlighting L/S attenuation as a reliable predictor of hepatic steatosis and fibrosis.

This study had several limitations. First, the sample size was relatively small ( $n = 51$ ), which may limit the generalizability of the findings. Second, it was a single-center study conducted in a tertiary care hospital, potentially introducing selection bias toward more severe cases. Third, only patients with Fibroscan values above 13 kPa were included, excluding those with mild fibrosis or early-stage NAFLD, which limits assessment across the full disease spectrum. Fourth, liver biopsy was not performed in all cases for histological confirmation, so Fibroscan and imaging correlations were used as surrogates for fibrosis staging. Finally, factors such as inter-observer variability in Doppler and imaging measurements and potential technical limitations of Fibroscan (e.g., obesity, skin-to-liver capsule distance) may have influenced results.

## 6. CONCLUSION

NAFLD is a significant and growing global health concern, with NASH representing its progressive form that can lead to advanced fibrosis and cirrhosis. While liver biopsy remains the gold standard, noninvasive methods like Fibroscan and Doppler-based measurements provide valuable, safer alternatives for assessing fibrosis. In our study, portal vein diameter, velocity, and HARI showed strong correlations with Fibroscan values, confirming their utility as noninvasive markers of advanced fibrosis. Monophasic hepatic vein waveform and elevated CRL values were associated with severe fibrosis, while liver-to-spleen attenuation effectively indicated early steatosis and progressive fibrosis. Overall, these findings support the use of combined noninvasive imaging and hemodynamic assessments to detect and stage NAFLD/NASH, enabling earlier intervention and improved management.

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