Role of Ultrasound Elastography in Characterizing Focal Liver Lesions with Pathological Correlation

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ABSTRACT

INTRODUCTION: Focal liver lesions (FLL) has been increasingly detected due to widespread imaging techniques and thus necessitates a thorough evaluation involving radiology, pathology, physical examination, and patient history. Ultrasonic elastography measures tissue elasticity helps differentiate between malignant and benign lesions. The primary objective is to evaluate the sensitivity and specificity of elastographic parameters in distinguishing malignant from benign liver tumors. Additionally to assess ultrasound elastographic parameters (stiffness value, stiffness ratio, and shear wave velocity) and to compare these parameters across different types of lesions, correlating them with pathological results.

MATERIALS AND METHODS: In a study of 60 patients with focal liver lesions, both grey scale and elastographic evaluations were conducted over 18 months at Sri Manakula Vinayagar Medical College. Diagnoses were confirmed via FNAC, biopsy, or cross-sectional imaging. The Receiver Operating Characteristic (ROC) curve was used to determine malignancy cutoff, with a p-value <0.05 considered significant. Data were analyzed using SPSS version 16.

RESULTS: Of 60 participants, 18 had benign lesions and 42 had malignancies. The mean stiffness (kPa) was 2.81 ± 1.24 for benign lesions and 6.47 ± 2.49 for malignant ones. The stiffness ratio averaged 4.08 ± 1.13 for benign and 8.63 ± 4.09 for malignant lesions. The mean shear wave velocity (SWV) was 0.90 ± 0.28 m/s for benign and 1.55 ± 0.63 m/s for malignant lesions. We identified a stiffness cutoff of 4.6 kPa, with 85.7% sensitivity and 94.4% specificity, and a stiffness ratio cutoff of 4.8, with 83.3% sensitivity and 77.7% specificity ($P \leq 0.01$). The SWV cutoff was 1.1 m/s, with 78.6% sensitivity and 83.3% specificity in distinguishing malignant from benign liver lesions.

CONCLUSION: This study helps to assess the utility of ultrasonic elastography in characterizing FLLs and supporting care decisions. Our study identified stiffness value as the most effective parameter.

KEYWORDS: Focal liver lesion, ultrasound elastography, stiffness value, stiffness ratio, shear wave velocity.

INTRODUCTION:

Focal liver lesions (FLL) are solid or cystic areas or masses in the liver that are recognized as abnormal. The term "lesion" is preferred over "mass" because it encompasses a broader range of abnormalities, including both solid and cystic masses. [1–3] Determining the characteristics of focal liver masses affects patient management in both health and disease and accounts for a sizeable portion of health care costs. In the world, primary liver cancer ranks as the fifth most frequent type of cancer [4] and the therapy of it depend heavily on imaging, which makes it possible to identify lesions more accurately when they are still tiny and treatable.

In the differential diagnosis, benign as well as malignant liver lesions should be taken into account. Therefore, it is crucial to manage FLLs with a comprehensive and organized approach. The most crucial element in assessing a liver lesion is a radiographic test. Conventional ultrasonography (US) is the first imaging modality used to screen for or investigate hepatic abnormalities. The characterization of FLL has been greatly enhanced by Color-Doppler and Contrast Enhanced Ultrasound (CEUS).

A recent imaging method to better describe the focal liver lesions is ultrasound elastography. It is a quick, simple, non-invasive, non-contrast-enhanced imaging technique that can be used for the patient's initial sonographic assessment. To select the most appropriate course of action, determining the type of liver lesion and first differentiating between malignant and benign lesions may be crucial diagnostic objectives.

Postmortem studies reveal that haemangiomas, the most prevalent benign liver tumor, are present in up to 20% of patients. Confirming their benignity with non- high-quality imaging techniques would prevent unnecessary biopsy discomfort [5,6].

The contrast-enhanced CT (CECT), ultrasonography, and MRI will provide specifics about the morphology of these lesions while elastography quantifies the natural ability of tissues to return to its original size and shape after deformation or stress. Inflammatory and neoplastic disorders can modify the stiffness of an organ's parenchyma by changing the tissues structure and composition [7-9]. These stiffness measurements will be used for assessing focal hepatic lesions and aids distinguishing between malignant and benign lesions.

Hence this study aimed to assess if ultrasonic elastography could effectively characterize liver lesions and guide care decisions.

MATERIALS AND METHODS

This study was a hospital based cross sectional study conducted in the Department of Radio diagnosis at Sri Manakula Vinayagar Medical College and Hospital (SMVMCH), Kalitheerthalkuppam, Puducherry, India which is located in a village 25km west of Puducherry, from September 2022 to February 2024. Considering the 87.5% specificity of the combined score of shear wave elastography measurements and ultrasonographic features to characterize focal liver lesions in a study by Wang W et al.[10] and the prevalence of focal liver lesions of 15.1% among hospital patients in the study by Kaltenbach T et al.,[11] and using the formula for calculating sample size for diagnostic test given by Buderer M et al.,[12] the sample size for this study was calculated to be 49 at 95% confidence interval. After adjusting for a 25% non-response rate the sample size was refined to be 61 and rounded off to 60, the nearest whole number. So 60 was the final sample size.

Patients of either sex with a clinical suspicion of focal liver lesions ,those previously diagnosed with focal liver lesions via Conventional CT/MRI, and individuals with focal liver lesions identified by ultrasound or Conventional CT/MRI were included in the study.

Patients with diffuse liver parenchymal disease without focal lesions, those with extrahepatic mass lesions infiltrating the liver, individuals with traumatic liver injury, pediatric patients, those already diagnosed with focal liver lesions and undergoing treatment, pregnant females regardless of gestational age, lesions deeper than 8 cm, patients with gross ascites, and uncooperative patients or those unable to hold their breath were excluded in this study.

BRIEF PROCEDURE:

Patients fulfilling the inclusion criteria were considered for the study. Patients were explained about the process of Ultrasonography and Elastography examination of focal liver lesion.

Ultrasound examination was performed with using Low frequency (2-5 MHz) probe in 70 G affiniti Ultrasound Machine. Conventional Ultrasound Imaging to be done to localize the liver lesion . Detected focal liver lesion were focused for Elastography evaluation. SWE acquisition was done after grey scale and Doppler vascularization examination of the liver. Liver stiffness was measured in areas without blood vessels during a 5-second breath hold at inspiration. For patients with multiple lesions, the largest lesion was selected as the index lesion.

Measurements were taken in two locations: the peripheral area of the largest lesion and the liver area more than 2 cm away from the lesion periphery (background liver). These measurements provided stiffness values (kPa), stiffness ratios, and shear wave velocity (m/s). Each measurement was performed five times for each group.

The mean value of five measurements for each individual was used in the statistical analysis. After the scoring and stiffness ratio is obtained, and is useful in discrimination between benign and malignant nodules .

After the evaluation by USG Elastography, the patient were followed with histopathological diagnosis by FNAC or Biopsy or cross -sectional imaging for correlation.

[Supplementary file with sample cases]

Statistical analysis:

Data was entered in Microsoft Excel and analysed using SPSS version 16. Categorical variables were represented using frequencies and percentages and Continuous variables were represented using mean and standard deviation. The categorical variables were analyzed using Chi-square test and continuous variables using independent t test. P value < 0.05 was considered as statistically significant at 95% confidence interval. Receiver Operative Characteristic curve was used to find the cut off for detecting malignancy with a P value < 0.05 considered as statistically significant.

Ethical consideration:

Institutional ethics committee approval was obtained (IEC no.EC/68/2022) and the study was conducted according to STARD checklist. Informed consent was obtained from participants in their native language.

RESULTS:

The Mean age of the study participants was 30.50 ± 14.46. The Chi-square test showed a significant association between age and diagnosis type, with malignant cases increasing with age. Among the study participants, 33 were female and 27 were male. Among participants with comorbidity, 5 were benign and 12 were malignant. In those without comorbidity, 13 were benign and 30 were malignant. This difference was not statistically significant by Chi square test.

Grey scale ultrasound characteristic of focal liver lesions are summarized in table 1.

Table 1: Ultrasound finding of focal liver lesion.

Ultrasound finding of focal liver lesion		Frequency	Percentage
Multiplicity of lesion	Single	31	51.7
	multiple	29	48.3
Ultrasound findings of background liver	Cirrhotic	2	3.3
	Normal	58	100
Echogenicity	Hypoechoic	41	68.3
	Hyperechoic	18	30
	Isoechoic	1	1.7
Vascularity	Increased	48	80
	Normal	12	20
Portal vein involvement	Yes	5	8.3
	No	55	91.7

Table 2: Diagnosis among the study participants

Diagnosis	Frequency	Percentage
Metastasis	24	40
Hepato Cellular Carcinoma	14	23.3
Hemangioma	12	20
Cholangiocarcinoma	4	6.7
Hepatic adenoma	3	5
Focal Nodular Hyperplasia	3	5
Total	60	100

By HPE diagnosis, 24 participants had metastasis, 14 had Hepato Cellular Carcinoma, 12 had hemangioma, 4 had Cholangiocarcinoma, 3 had Hepatic adenoma and 3 had Focal Nodular Hyperplasia.

Table 3: Association between various ultrasound findings of focal liver lesion and malignancy among study participants.

Ultrasound finding of focal liver lesion		Benign	Malignant	Chi square value	P value
Multiplicity of lesion	Single	18	13	24.05	**0.001***
	multiple	0	29		
Ultrasound findings of background liver	Cirrhotic	0	2	0.88	0.34
	Normal	18	58		
Echogenicity	Hypoechoic	2	39	39.03	**0.001***
	Hyperechoic	15	3		
	Isoechoic	1	0		
Vascularity	Increased	6	42	35.00	**0.001***
	Normal	12	0		
Portal vein involvement	Yes	0	5	2.33	0.12
	No	18	37		

*- statistically significant by Chi square test

Multiplicity of lesion, echogenicity and presence of vascularity in focal liver lesion showed statistically significant association with malignancy.

Table 4: Association between various Elastographic parameters and malignancy among the study participants

Elastographic parameters	**Benign**	**Malignant**	**Independent t test value**	**P value**
Stiffness (kPa) **[Mean ± SD]**	2.81 ± 1.24	6.47 ± 2.49	5.89	**0.001***
Stiffness Ratio[**Mean ± SD]**	4.08 ± 1.13	8.63 ± 4.09	3.50	**0.001***
Shear Wave Velocity (m/s)[**Median ± IQR]**	0.90 ± 0.28	1.55 ± 0.63	4.10	**0.001***

*- statistically significant by independent t test

All elastographic parameters in focal liver lesion showed statistically significant association with malignancy.

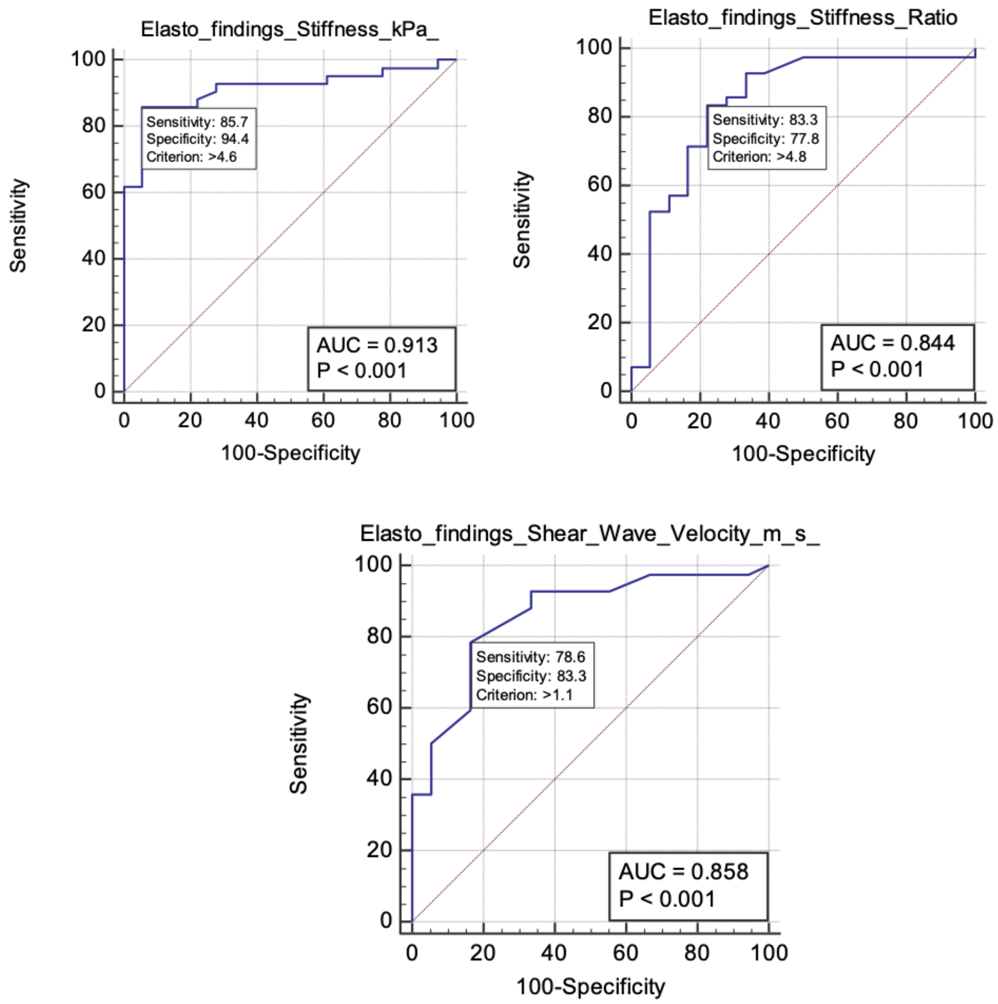

Figure 4: ROC of various elastographic parameters in detecting malignancy among the study participants

ROC curve analysis revealed the following cut-off values: Elastographic stiffness at 4.6 kPa with 85.7% sensitivity and 94.4% specificity; Elastographic stiffness ratio at 4.8 with 83.3% sensitivity and 77.7% specificity; and Elastographic shear wave velocity at 1.1 with 78.6% sensitivity and 83.3% specificity.

DISCUSSION

Our research aimed to assess the efficacy of various elastographic indicators (such as Stiffness value, Stiffness Ratio, Shear wave velocity) in distinguishing benign and malignant liver lesions.

Within our study cohort, 68% of patients exhibited hypoechoic liver lesions, and we identified a statistically significant correlation indicating that these hypoechoic lesions were likely malignant. ie) 95% of the hypoechoic lesions were malignant.

A significant association has been demonstrated between malignant lesions exhibiting increased internal vascularity in our study. (Table 3)

Our study findings revealed that portal vein involvement was observed solely in malignant lesions, with approximately 63% of these lesions showing no signs of such involvement. (Table 3)

Table 5: Comparison of mean stiffness values for each focal liver lesion in our study with a comparison study.

FOCAL LIVER LESION	OUR STUDY	Qiang Lu et al.[13]
Hemangioma	2.1 (range,1.82-2.52)	9.3 (range,3.1-41)
Hepatic adenoma	3.6 (range,0.31-6.88)	-
Focal nodular hyperplasia	4.59 (range,1.43-7.75)	10 (range, 2.9-26)
Hepatocellular carcinoma	6.3 (range ,5.9-7.00)	34 (range, 4.4 -188)
Cholangiocarcinoma	8.37 (range ,0.7-16.04)	25 (range, 5.5-79)
Metastasis	6.22 (range , 5.14-7.31)	30 (range, 4.7-64)
Cirrhotic nodules	-	11 (range, 4.4 -49)

These results reveal minor inconsistencies when compared to the study mentioned earlier. It's important to acknowledge that making direct comparisons with prior research is difficult due to differences in the populations studied.

In our research, we identified a cutoff value of 4.6kPa for Stiffness value, with a sensitivity of 85.70% and specificity of 94.4%. Similarly, for Stiffness Ratio, we determined a cutoff value of 4.8 yielding a sensitivity of 83.3% and specificity of 77.7% in distinguishing between malignant and benign liver lesions (P value ≤ 0.01). (Table 5)

Qiang Lu et al.[13] found that malignant tumors had notably higher stiffness values and stiffness ratios compared to benign lesions (P < .0001 and P = .0003, respectively). When distinguishing between malignant and benign lesions, diagnostic accuracy using stiffness values was significantly better than using stiffness ratios (AUC, 0.86 vs 0.69; P < .001). They established a stiffness value cutoff of 13 kPa with 78% sensitivity and 83% specificity, while a stiffness ratio cutoff of 1.3 yielded 79% sensitivity and 45% specificity.

Yu et al.[14] found a significant distinction in stiffness values between 41 benign and 64 malignant lesions (P < .001), with a sensitivity of 68% (28 out of 41) and specificity of 69% (44 out of 64).

Utilizing quantitative acoustic radiation force impulse imaging technology, Heide et al.[15] demonstrated statistically comparable stiffness values between 38 benign lesions and 24 malignant tumors (P = .28).

The study conducted by Qiang Lu et al.[13] confirmed that the stiffness value could serve as a non-invasive predictor for malignancy in focal liver lesions. In differentiating malignant from benign liver lesions using stiffness values, the sensitivity and specificity were 78% (156 out of 159) and 83% (48 out of 58), respectively.

Our study revealed the cutoff value for SWV was determined to be 1.1m/s, with a sensitivity of 78.6 % and a specificity of 83.30% in differentiating malignant from benign masses.(Table 5)

Guo et al.[16] assessed the mean shear wave velocity (SWV) differences in focal liver lesions, finding SWV values of 2.95 ± 1.00 m/s for malignant lesions and 1.69 ± 0.89 m/s for benign ones ($P < 0.001$). They suggested a cutoff value of 2.13 m/s for distinguishing between malignant and benign masses. Similarly, our study found significantly higher mean SWV values in malignant liver lesions compared to benign ones ($P < 0.01$).

Despite the significant differences in the mean values of elastographic parameters between benign and malignant liver lesions ($P \leq 0.01$), in our study the stiffness value proved to be the most effective parameter for distinguishing between malignant and benign liver lesions.

Our study's limitations include a small sample size of benign lesions, comprising of 12 hemangiomas, 3 focal nodular hyperplasias, and 3 hepatic adenomas which potentially affects the accuracy of results and necessitates validation through larger studies. Additionally, we did not assess interobserver variability. The findings may lack generalizability due to the single-center approach, and ultrasound elastography encountered issues like poor patient compliance and operator dependence.

CONCLUSION

Ultrasound elastography is a non-invasive technique that measures liver lesion stiffness, adding valuable data to conventional ultrasound and aiding in the differentiation of liver lesions. Our study demonstrated its effectiveness in distinguishing malignant from benign lesions, with stiffness value being the most reliable parameter. Despite its potential, further large-scale studies are needed to fully establish its role. Integrating elastography with conventional ultrasound allows for a thorough assessment of liver tumors, which could enhance targeted treatment strategies.

ABBREVIATIONS

FLL	Focal liver lesion
USG	Ultrasound sonography
FNAC	Fine needle aspiration cytology
SPSS	Statistical Package for social science
SWV	Shear wave velocity
CEUS	Contrast enhanced Ultrasound
CT	Computed Tomography
CECT	Contrast Enhanced Computed Tomography
MRI	Magnetic Resonance Imaging
FNH	Focal Nodular Hyperplasia
HCC	Hepatocellular carcinoma
HCA	Hepatocellular adenoma
USE	Ultrasound Elastography
SWI	Shear Wave Imaging

AUROC	Area under the receiver operating characteristic curve
HPE	Histopathological Examination

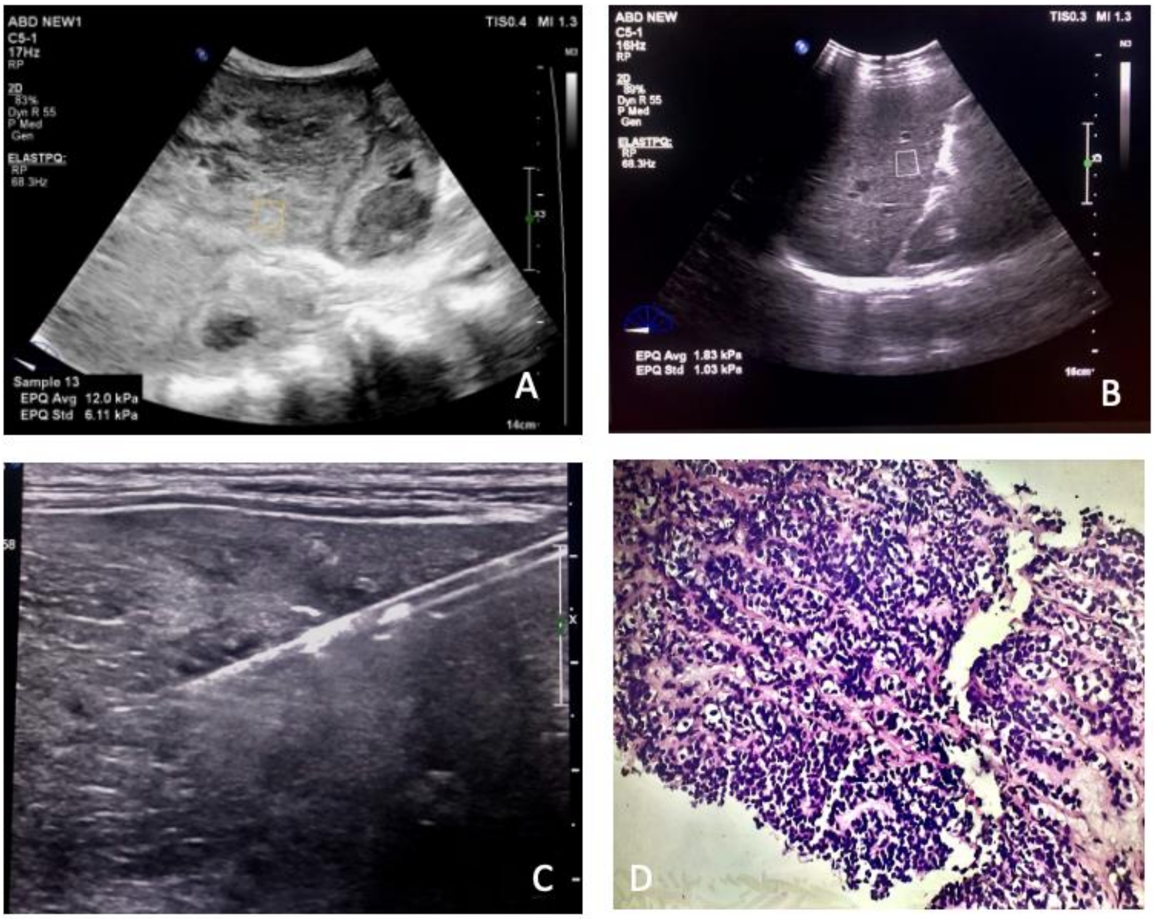

Figure 1: 65 years old female, a known case of carcinoma cervix, came with complaints of abdominal pain diagnosed to have heteroechoic liver lesion on USG. Ultrasound elastography image (A) showed average Stiffness value of lesion was 10.9kPa , Stiffness value of background liver(B) was 1.83kPa.Stiffness ratio was 5.9. Average shear wave velocity was 1.82m/s USG guided biopsy(C) was performed. Histopathology showed metastatic carcinoma(D).

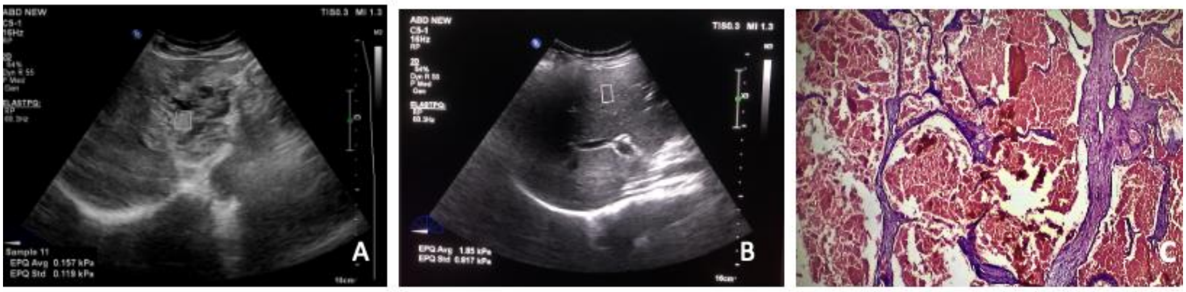

Figure 2: 40 years old female came with complaints of epigastric pain and on USG, focal, well defined, hyperechoic hepatic lesion was found. Ultrasound elastography image (A) showed average Stiffness value of lesion was 1.7kPa, Stiffness value of background liver(B) was 1.8kPa. Stiffness ratio was 0.94. Average shear wave velocity was 0.69m/s. Histopathology showed Cavernous hemangioma (C).

Figure 3: 52 years old male came with complaints of upper abdominal pain and found to have a hypoechoic liver lesion on USG. Ultrasound elastography image (A) showed average Stiffness value of lesion was 8.03kPa, Stiffness value of background liver(B) was 0.39kPa. Stiffness ratio was 20.5. Average shear wave velocity was 1.5 m/s. Histopathology showed Hepatocellular carcinoma(C).

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