Original Article

Role of Acoustic Radiation Force Impulse Elastography in the Characterization of Focal Solid Hepatic Lesions

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ABSTRACT

Objective: The purpose of the study is to investigate the usefulness of acoustic radiation force impulse (ARFI) elastography in the characterization of focal solid liver lesions as benign, malignant, or metastatic using ARFI two-dimensional (2D) imaging and ARFI quantification (shear wave velocities [SWVs]). **Materials and Methods:** Sixty lesions were included in this study. The lesions were classified into three groups: Group I included benign lesions (n = 25), Group II included malignant lesions (n = 27), and Group III included metastatic lesions (n = 8). ARFI elastography was performed in all these patients using a Siemens ACUSON S 2000™ ultrasound machine. Stiffness and size of the lesions were assessed on ARFI 2D images in correlation with B-mode ultrasound images. SWVs were obtained in these lesions for the quantification of stiffness. **Results:** In ARFI 2D images, malignant lesions were predominantly stiffer and larger, while benign lesions were softer and similar in size ($P < 0.05$). The mean SWVs in benign, malignant, and metastatic lesions were 1.30 ± 0.35 m/s, 2.93 ± 0.75 m/s, and 2.77 ± 0.90 m/s, respectively. The area under receiver operating characteristic curve of SWV for differentiating benign from malignant lesions was 0.877, suggesting fair accuracy (95% confidence interval: 0.777–0.976); with a cutoff value of 2 m/s, showing sensitivity: 92%; specificity: 96%; positive predictive value: 96%; negative predictive value: 93% ($P < 0.05$). Statistically significant difference exists in SWV of benign and malignant or metastatic lesions. **Conclusion:** ARFI elastography with 2D imaging and quantification might be useful in the characterization of benign and malignant liver lesions.

Keywords: *Acoustic radiation force impulse, elasticity imaging, elastography, liver tumors, shear wave velocities*

Introduction

Characterization of focal liver lesions (FLLs) is a common problem in clinical and radiologist's practice. Early characterization of these lesions is essential to formulate optimal treatment strategy and to achieve better outcomes in these patients. Although ultrasonography, the first-line modality in the evaluation of these lesions, is highly sensitive and specific in the differentiation of cystic and solid lesions, its role in the characterization of solid lesions is limited due to nonspecific sonographic features of benign and malignant lesions.[1-3] This necessitates further evaluation of majority of these lesions by contrast-enhanced ultrasonography, contrast-enhanced computed tomography, and magnetic resonance imaging (MRI) for further characterization, which not only increases the diagnostic cost and waiting times but also involves risks of contrast administration and radiation exposure. Despite the availability of many noninvasive imaging methods, till date, biopsy remains the gold standard for the characterization of solid liver lesions.[4,5]

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Ultrasound elastography has emerged as an important adjunct to conventional ultrasound in recent times and has been reported to be useful for the characterization of various tumors, which are usually stiffer than normal tissues. Although manual compression techniques are popular in the evaluation of the breast masses,[6,7] prostate cancer,[8,9] and thyroid nodules,[10] their application had been difficult in the liver as it is surrounded by the rib cage. With the advent of acoustic radiation force impulse (ARFI) elastography, which uses "motorized compression" by producing short acoustic push pulses to assess the target tissue displacement and stiffness, apart from qualitative features such as stiffness, size, and conspicuity of lesions, quantification of stiffness was made possible in terms of shear wave velocity (SWV) in the lesion.[11,12]

Since Fahey et al., 2008[13] showed the usefulness of ARFI elastography in characterizing the FLLs, majority of the studies evaluated only SWV in FLLs.[14-25] Very few studies have comprehensively evaluated both qualitative and quantitative parameters together.[26,27] The rationale behind this study is a comprehensive evaluation of FLLs on both qualitative and quantitative ARFI techniques and to assess the role and efficacy of ARFI elastography in the characterization of solid FLLs based on appearances in elastogram images and SWV (ARFI elastometry).

Materials and Methods

The study was conducted as a prospective controlled analytical study in a tertiary care setup. The institutional review board of our hospital approved the study and waived the consent for elastography examination. Ninety-four patients who presented to our department between January 2014 and January 2016 for the evaluation of solid FLLs were included in the study. Patients with diffusely infiltrative lesions and subcentimeter lesions were excluded. Thirty-four patients were excluded due to either technical failure such as patient motion (3 patients), presence of a deep-seated lesion (10 patients) or patient's inability to hold their breath properly (11 patients), and patients who did not undergo histopathological examination or other confirmatory imaging (10 patients). The final study population consisted of 60 patients with either single or multiple lesions.

Various lesions included in the study are shown in Table 1. Size, stiffness, and margins of the lesions were assessed on ARFI elastogram images in relation to the corresponding B-mode image. SWVs were assessed using ARFI elastometry. SWVs were also obtained in thirty age- and sex-matched controls which served as a reference for the normal population. After

Table 1: Various pathologies included in the study and their categorization into three groups

Group of lesions	Total number of lesions	Final pathological diagnosis
Group I (benign lesions)	25	Hemangiomas-21
		Organized abscesses-2
		Hepatic adenoma-1
		Tuberculous granulomas-1
Group II (malignant lesions)	27	HCC-22
		Cholangiocarcinoma-3
		Fibrolamellar carcinoma-1
		AML infiltrates-1
Group III (metastatic lesions)	8	Colon carcinoma-4
		Gastric adenocarcinoma-1
		Gallbladder carcinoma-1
		Rectal carcinoma-1
		TCC of ureter-1

TCC: Transitional cell carcinoma, HCC: Hepatocellular carcinoma, AML: Acute myeloid leukemia

ultrasonography for the evaluation of echotexture and exclusion of fatty changes, SWVs were obtained in different segments of liver for four times and the mean SWVs were calculated for this control population.

One of the examiners with 5 years of experience in the conventional ultrasound performed ARFI elastography on a Siemens ACUSON S 2000 ultrasound machine using a 2–4 MHz (4C1) curved array transducer, operating at 4 MHZ. After fitting the ARFI image box to fully cover the lesion, a two-dimensional (2D) ARFI elastogram image was obtained (Virtual Touch™ tissue imaging) with a corresponding B-mode image displayed by its side. In patients where the lesion was larger, the region of interest (ROI) was chosen as to partly include the lesion and its margins as well. Multiple ROIs were thus used to cover the whole lesion. The SWVs (expressed in meters per second), using Virtual Touch™ tissue quantification (ARFI elastometry), was obtained with ROI placed over the lesion, through right intercostal or subcostal approach with a short period of breath hold. In patients with multiple liver lesions (13 of 60 patients), the largest of the lesions in the right lobe of liver amenable for both elastometry and biopsy was chosen. The velocities were obtained four times in each lesion and were averaged.

Two radiologists, blinded to pathological diagnosis, independently reviewed the 2D ARFI elastogram images on PACS viewer stations (GE Centricity 5.0 PACS Workstations) in correlation with the corresponding B-mode image for qualitative parameters such as stiffness and size. Images were reviewed by the radiologists in random sequence after 6 months to avoid recall bias. Any discrepancies between the two reviewers were resolved through consensus. The lesions were categorized as stiffer (darker), similarly stiff (of similar darkness), or softer (brighter) based on the lesion's brightness relative to the background liver on ARFI images. Based on the size, the lesions were classified as larger, smaller, or of similar in size as that of the B-mode image by visual inspection.

The hemangiomas were diagnosed based on a combination of the typical findings on CT and MRI scans.[28] Hepatocellular carcinoma (HCC) was confirmed by histopathology in 18 patients and by clinical diagnosis in four patients according to the American Association for the Study of Liver Disease 2005 recommendations.[29-31] Rest of the benign, malignant, and metastatic lesions were confirmed by histopathology. The origins of metastatic lesions were determined by corroborative evidence of primary malignancy on other imaging modalities.

The results were analyzed in correlation with final pathological diagnosis and the patients were assigned into three groups. Group I consisted of benign lesions. Group II consisted of primary malignant liver lesions. Group III consisted of metastases.

Statistical analysis

All continuous variables were represented by mean with standard deviation, accompanied by range and median. Categorical data were reported as absolute number of patients and percentage of the group studied. Pearson Chi-square test or Fischer's exact test was used to compare categorical data. The differences among the mean SWVs in various groups of FLLs were evaluated using analysis of variance test. The accuracy of SWV values in the differentiation of benign and malignant lesions was evaluated by calculating sensitivity, specificity, and positive and negative predictive values. Receiver operating characteristic (ROC) curve and areas under the ROC (AUROC) were used to estimate the diagnostic performance. The cutoff value was determined by considering the highest sum of sensitivity and specificity. $P < 0.05$ was considered as statistically significant. The statistical analysis was performed using the SPSS software version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

The mean age of the study population was 52.2 years, with age ranging from 20 to 73 years. The most common age group was 51–60 years; 67% were males (40 of 60) and 33% were females (20 of 60), with a male:female ratio of 2:1. Of 60 patients, 47 patients (78.3%) had single lesions in the liver, while 13 patients (21.7%) had multiple lesions in the liver. Of 60 patients, 40 patients (66.6%) had normal surrounding liver echotexture on ultrasonography. Echotexture changes of cirrhosis were noted in 20 patients (33.3%). The mean SWV in control population was 1.17 m/s.

Stiffness of the lesion

Characterization of the FLLs based on stiffness in ARFI elastography images into various groups is shown in Table 2. This study showed that a benign lesion will predominantly be softer (40%) or similarly stiff (20%) as that of surrounding liver, while a malignant or metastatic lesion will predominantly be stiffer (92% and 87%, respectively) [Table 3]. Moreover, a lesion that is either softer or similarly stiff as surrounding liver has significantly higher chance of being benign (90% and 83%, respectively). A stiffer lesion may not be reliably differentiated, while it has a higher chance of being malignant (67%). There was statistically significant difference between the three groups in terms of stiffness on ARFI elastography images ($P < 0.0001$).

Size of the lesion

Characterization of the FLLs based on size in ARFI elastography is shown in Table 4. This study showed that a benign lesion on ARFI elastography appears either similar in size (88%) or smaller. Malignant and metastatic lesions appear predominantly larger in size on ARFI elastography (74% and 62%, respectively) or less often of the same size (26% and 38%, respectively). Similarly, a lesion that is smaller on ARFI elastography is almost always benign (100% specificity), while a lesion that is larger is almost always malignant (80%) or metastatic (20%). A lesion that is of the same size on ARFI elastography cannot be reliably characterized though it has a higher chance of being benign (68%). Statistically significant difference exists between the three groups in terms of tumor size evaluated on ARFI elastography images ($P < 0.0001$) [Table 5].

Shear wave velocities

The mean and median SWV for various tumor groups are shown in Table 6. The mean SWVs in benign, malignant, and metastatic lesions were 1.30 ± 0.35, 2.93 ± 0.75, and 2.77 ± 0.90 m/s, respectively. The mean SWV in the Group I (benign lesions) was significantly lower than that in Group II and Group III ($P < 0.0001$) [Figure 1]. There was considerable overlap in the SWVs of Group II and Group III. The SWVs in various lesions are shown in Table 7 [Figures 2-8]. The mean SWVs of surrounding liver in benign, malignant, and metastases were 1.27 ± 0.13, 1.60 ± 0.29, and 1.42 ± 0.27 respectively, which did not show statistically significant difference.

The AUROC of SWVs for differentiating benign from malignant lesions was 0.877, suggesting

Table 2: Characterization of various lesions based on their appearance on stiffness on acoustic radiation force impulse elastographic images

Stiffness of lesions on ARFI elastography	Group I (benign lesions)	Group 2 (malignant lesions)	Group 3 (metastatic lesions)
Stiffer	Hemangiomas-5	HCCs-20	Colon carcinoma-4
		Cholangiocarcinomas-3	Gallbladder carcinoma-1
		Fibrolamellar carcinoma-1	Rectal carcinoma-1
		Leukemic infiltrates - 1	TCC ureter-1
Similar stiffness	Hemangiomas-9	HCC-1	Carcinoma stomach-1
	Hepatic adenoma-1		
Softer	Hemangiomas-7	HCC-1	0
	Organized abscesses-2		
	TB granulomas-1		

ARFI: Acoustic radiation force impulse, TCC: Transitional cell carcinoma, TB: Tuberculosis, HCCs: Hepatocellular carcinomas

Table 3: Comparison of stiffness of the lesion on two-dimensional acoustic radiation force impulse elastography with final diagnosis

Stiffness	Final diagnosis			Total	*P*
	Group 1 (benign lesions)	Group 2 (malignant lesion)	Group 3 (metastatic lesions)		
Stiffer	5 (20)	25 (92.5)	7 (87.5)	37 (61.7)	<0.0001*
Similar stiffness	10 (40)	1 (3.7)	1 (12.5)	12 (20)	
Softer	10 (40)	1 (3.7)	0	11 (18.3)	
Total	25 (100)	27 (100)	8 (100)	60 (100)	

Numbers in the table represent the absolute number of lesions in each group, percentages are shown in parenthesis. *Pearson Chi-square test was used to assess the statistical significance

Table 4: Characterization of various lesions based on their appearance on size on acoustic radiation force impulse elastographic images

Size of lesions on ARFI elastography	Group I (benign lesions)	Group 2 (malignant lesions)	Group 3 (metastatic lesions)
Same size	Hemangiomas-18	HCCs-4	Gallbladder carcinoma-1
	Hepatic adenoma-1	Cholangiocarcinoma-1	Carcinoma stomach-1
	Organized abscesses -2	Fibrolamellar carcinoma-1	TCC ureter-1
	TB granulomas-1	Leukemic infiltrates-1	
Larger	0	HCC-18	Colon carcinoma-4
		Cholangiocarcinoma -2	Rectal carcinoma-1
Smaller	Hemangiomas-3	0	0

ARFI: Acoustic radiation force impulse, TCC: Transitional cell carcinoma, TB: Tuberculosis, HCCs: Hepatocellular carcinomas

Table 5: Comparison of size of the lesion on two-dimensional acoustic radiation force impulse elastography with final diagnosis

Size of the lesion on ARFI	Final diagnosis			Total	*P*
	Group 1 (benign lesions)	Group 2 (malignant lesion)	Group 3 (metastatic lesions)		
Same	22 (88)	7 (25.9)	3 (37.5)	32 (53.3)	<0.0001*
Larger	0	20 (74.1)	5 (62.5)	25 (41.7)	
Smaller	3 (12)	0	0	3 (5)	
Total	25 (100)	27 (100)	8 (100)	60 (100)	

Numbers in the table represent the absolute number of lesions in each group. Percentages were represented in parenthesis. *Pearson Chi-square test was used to assess the statistical significance. ARFI: Acoustic radiation force impulse

fair accuracy (95% confidence interval: 0.777–0.976) [Figure 9]. The best cutoff value for SWV, chosen based on the highest combination of sensitivity and specificity (92.6% and 81.2%, respectively), was 2 m/s. The accuracy for differentiation of benign and malignant lesions for the cutoff of 2 m/s is as follows [Table 8]: sensitivity: 92%; specificity: 96%; positive predictive value: 96%; negative predictive value: 93% ($P < 0.000001$). The accuracy for differentiation of benign and metastatic lesions for cutoff of 2 m/s is as

Table 6: Analysis of shear wave velocities in various groups of lesions

	Analysis of SWV (ARFI elastometry)			*P*
	Group 1 (benign lesions)	Group 2 (malignant lesion)	Group 3 (metastatic lesions)	
Mean±SD	1.3016±0.357942	2.934074±0.750309	2.77±0.901443	<0.0001*
Median	1.21	3.02	2.37	
Range	0.62-2.08	0.94-4.61	1.91-4.42	

Values in table represent shear wave velocities measured in m/s. *ANOVA test was used to assess the significance of variance between means in three groups of lesions. SD: Standard deviation, SWV: Shear wave velocity, ANOVA: Analysis of variance, ARFI: Acoustic radiation force impulse

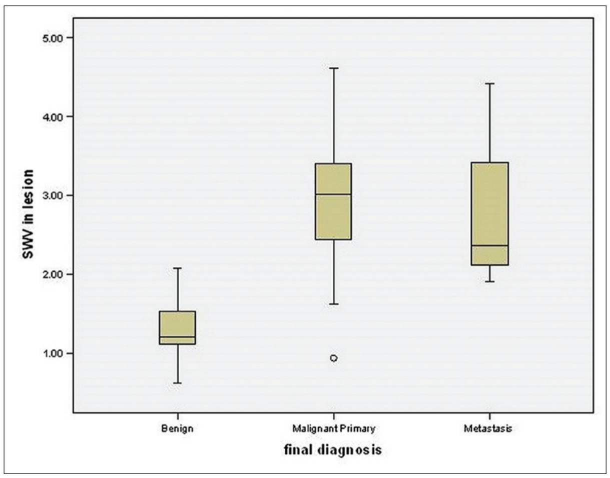

Figure 1: Box-whisker plot chart comparing the mean shear wave velocities (m/sec, y-axis) between the three groups of lesions (x-axis). Upper and lower limits of the box represent first and third quartiles, respectively, in each group. The central line represents the mean shear wave velocities for each group.

follows [Table 9]: sensitivity: 96%, specificity: 87.5%, positive predictive value: 96%, negative predictive value: 87.5%; *P* value: 0.000014. No significant difference was noted between the SWV of malignant and metastatic lesions (*P* = 0.553094).

Discussion

ARFI elastography of FLLs was first described by Fahey et al., 2008,[13] who showed that HCCs were softer than the regional cirrhotic liver parenchyma, but the metastases were stiffer than regional noncirrhotic liver parenchyma. Two studies by Cho et al.,[26] and Kim et al.,[27] had comprehensively evaluated stiffness and SWV in FLLs although the latter study is the only study to evaluate size of the lesion on ARFI elastography.

Stiffness of the lesion

This study showed that a benign lesion will predominantly be either softer or equally stiff as of surrounding liver, while a malignant/metastatic lesion will usually be stiffer than surrounding liver. These findings can be explained from the pathological point of view that malignant lesions having higher cellularity tend to be stiffer, while benign lesions such as hemangiomas which are composed of sinusoids tend to have lower stiffness. The results were

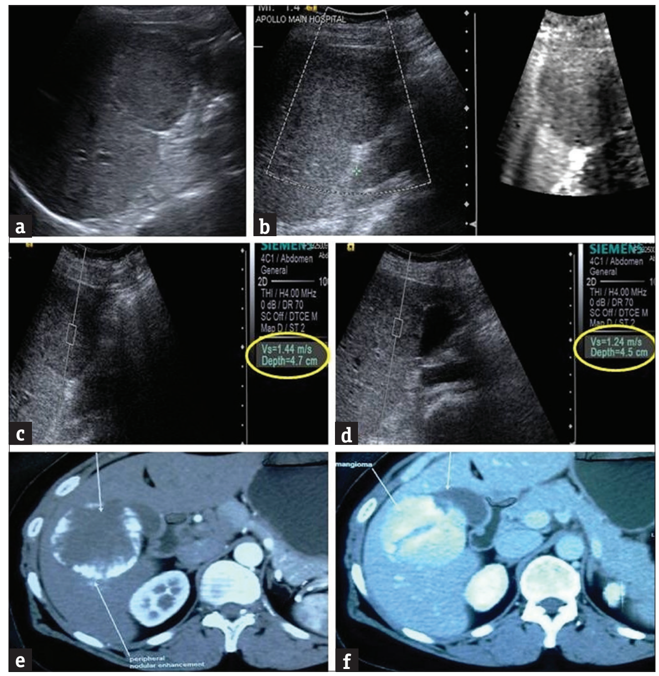

Figure 2: A 42-year-old-female patient with incidentally detected homogenously hypoechoic lesion in noncirrhotic liver (a). Acoustic radiation force impulse elastography showing that the lesion is minimally stiffer than the surrounding liver and similar in size as that of B-mode (b). Acoustic radiation force impulse elastometry showing mean shear wave velocity of 1.32 m/s (c and d). Contrast-enhanced computed tomography scan revealed peripheral nodular enhancement of the lesion on arterial phase and centripetal filling in of contrast in portal venous phase, confirming hemangioma (e and f).

not consistent with those of Cho et al.,[26] and Kim et al.,[27] as the former study had a similar number of stiffer tumors and softer tumors in both the groups, while the latter study failed to show statistical significance. This discrepancy might be due to the different nature of the pathologies included in various groups and differences in the severity of cirrhosis of background liver in each study population. While all the patients with HCC in the study by Cho et al.,[26] had chronic liver disease, only 20 of 27 patients with HCC had features of overt cirrhosis on ultrasound in this study. Regarding stiffness of metastatic tumors, the results are consistent with that of Cho et al.[26]

Size of the lesion

The rationale behind evaluation of size is that the infiltrative margins of malignant lesions show an apparent

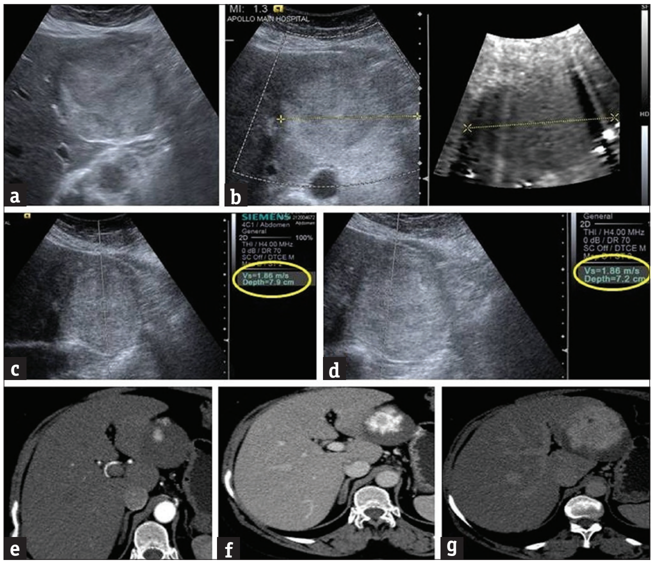

Figure 3: A 56-year-old female patient with a large well-defined heteroechoic mass lesion in noncirrhotic left lobe of liver (a). Acoustic radiation force impulse elastography showing that the lesion is mildly stiffer than the surrounding liver and similar in size as that of B-mode (b). Acoustic radiation force impulse elastometry reveals that the shear wave velocity in the lesion is mildly higher than surrounding parenchyma (mean shear wave velocity: 1.86 m/s) (c and d). Contrast-enhanced computed tomography scan showing peripheral nodular enhancement in arterial phase, centripetal fill-in of contrast and opacification in delayed phase, typical of hemangioma (e-g).

Table 7: Shear wave velocities in various lesions included in the study

Lesions (*n*)	SWVs (m/s)	Remarks
Benign lesions		
Hemangiomas (21)	Range: 0.62-2.08 Mean: 1.34±0.35	One hemangioma had SWV of >2 m/s (2.08 m/s)
Adenoma (1)	1.34	-
Granulomas (1)	0.9	-
Abscess (2)	0.89, 0.88	-
Malignant lesions		
HCC (22)	Range: 0.94-4.61 Mean: 2.95±0.80	Two HCCs had SWV of <2 m/s (0.94 and 1.62 m/s)
Cholangiocarcinoma (3)	Range: 2.44-3.64 Mean: 2.93±0.62	-
Fibrolamellar carcinoma (1)	2.74	-
AML infiltrates (1)	2.73	-
Metastases		
Colon carcinoma-4	Range: 2.17-4.42 Mean: 3.13±1.11	-
Gastric adenocarcinoma-1	1.91	SWV <2 m/s
Gallbladder carcinoma-1	3.12	-
Rectal carcinoma-1	3.72	-
TCC of ureter-1	2.08	-

SWV: Shear wave velocity, TCC: Transitional cell carcinoma, HCC: Hepatocellular carcinoma, AML: Acute myeloid leukemia

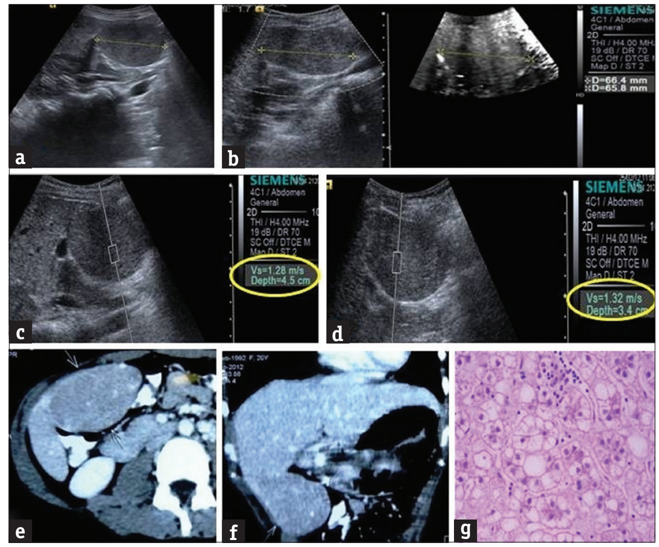

Figure 4: A 30-year-old female with incidentally found well defined isoechoic exophytic lesion from segment IV of liver (a). Acoustic radiation force impulse elastography showing that the lesion is similar in stiffness as of surrounding liver and of similar size as that of B-mode image (b). Acoustic radiation force impulse elastometry showing comparable shear wave velocity to normal liver (mean shear wave velocity: 1.34 m/s) (c and d). Computed tomography scan showing enhancing well-encapsulated benign mass arising from liver (e and f). Postexcision biopsy showing hepatic adenoma (g).

increase in size on elastogram images. This study showed that smaller lesion is always benign (100%) while a lesion that is larger on ARFI elastography is almost always malignant (80%) or metastatic (20%). The results did not correlate with the only attempted previous study by Cho et al.,[26] which failed to show significant difference in terms of size. Further studies with larger series are required to test the consistency of these findings.

Shear wave velocities

The comparison of mean SWV in various groups of lesions in this study with the previous studies is shown in Table 10. The mean SWV for benign lesions in this study was lowest (1.30 m/s) among all the studies and is closely comparable to studies by Zhang et al.,[18] and Davies and Koenen[15] (1.33 m/s and 1.35 m/s, respectively), unlike the report by Frulio et al.,[19] which was significantly higher than other studies (2.53 m/s) due to higher number of adenomas and focal nodular hyperplasia (FNH) in the benign group. This variation can partly be explained by varying pathological compositions of hemangiomas as well.

The mean SWV for malignant lesions in this study (2.93 m/s) is comparable to various other studies,[14-19] which ranged between 2.24 and 3.16 m/s. Two HCCs having SWVs of 0.94 and 1.62 m/s were softer and similar in stiffness in ARFI elastogram images. The mean SWV for metastatic lesions in this study was 2.77 m/s, with a range of 1.91–4.42 m/s, which

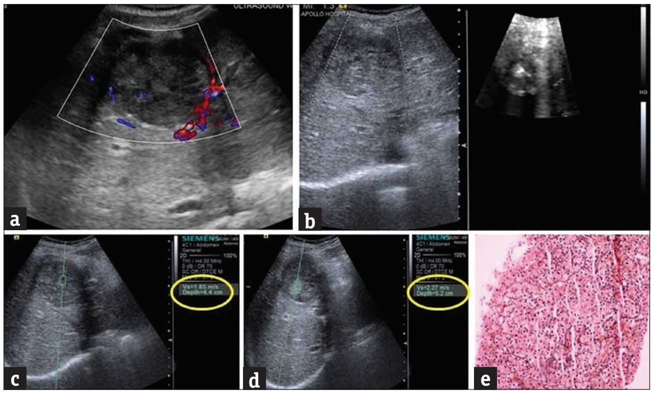

Figure 5: A well-defined heteroechoic lesion in 45-year-old alcoholic with minimal coarse echotexture in surrounding liver (a). Acoustic radiation force impulse elastography showing the lesion is of mixed stiffness with few stiffer areas and few softer areas and of similar size as of B-mode image (b). Acoustic radiation force impulse elastometry from the lesion (stiffer areas) showing mean shear wave velocity of 2.21 m/s in the lesion (c and d). Histopathology showing that the lesion is hepatocellular carcinoma (reticulin stain) (e).

Table 8: Assessment of accuracy of the cutoff shear wave velocity of 2 m/s (shear wave velocity) for differentiation between benign and malignant lesions

Final diagnosis	SWV in lesions		Total	P
	<2 m/s	>2 m/s		
Benign	24	1	25	<0.0001*
Malignant primary	2	25	27	
Total	26	26	52	

*Fisher's exact test was used to assess the statistical significance. SWV: Shear wave velocity

Table 9: Assessment of accuracy of the cutoff shear wave velocity of 2 m/s (shear wave velocity) for differentiation between benign and metastatic lesions

Final diagnosis	SWV in lesions		Total	P
	<2 m/s	>2 m/s		
Benign	24	1	25	<0.0001*
Metastatic	1	7	8	
Total	25	8	33	

*Fisher's exact test was used to assess the statistical significance. SWV: Shear wave velocity

is comparable to most of the previous studies.[14-19,26,27] Elasticity–pathology correlations of liver tumors by Frulio et al.,[19] showed that necrosis can reduce the stiffness of metastatic lesions. Studies with larger number of lesions and pathological correlations are required to establish the characteristics that affect stiffness and SWVs.

This study showed statistically significant difference between mean SWV of benign lesions and malignant or metastatic lesions. No significant difference was observed in SWV between malignant and metastatic groups. These findings are consistent with most of the previous studies which showed statistical significance in terms of SWV in

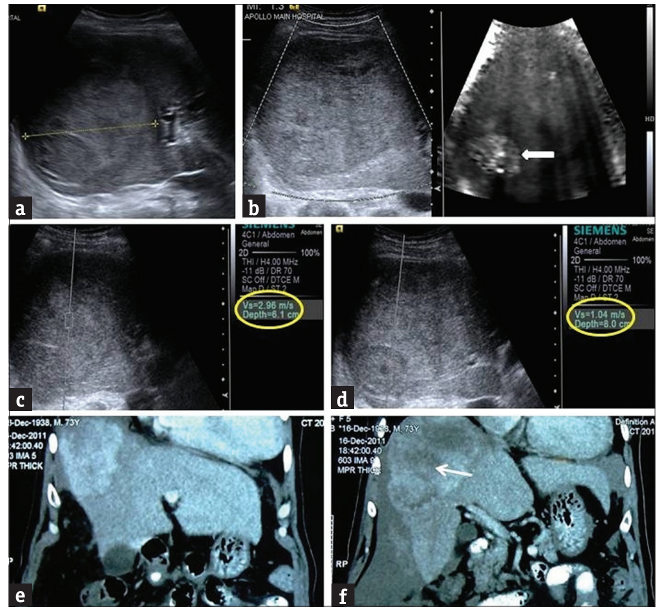

Figure 6: A 73-year-old male patient with large ill-defined heteroechoic lesion on ultrasonography in cirrhotic liver (a). Acoustic radiation force impulse elastogram reveals the lesion similar in size, stiffer than the surrounding liver with few softer areas (thick white arrow) suggesting necrosis (b). The shear wave velocity is higher in stiffer areas (mean shear wave velocity: 2.92 m/s) and very low in the softer areas (mean shear wave velocity: 1.04 m/s) (c and d). Contrast-enhanced computed tomography scan showing heterogeneously enhancing mass (hepatoma) in the right lobe of liver with necrosis (thin white arrow) (e and f).

the differentiation of benign and malignant lesions.[14-19] Two previous studies by Frulio et al., and Sendroiu et al.,[19,20] which failed to show significant difference in SWV had a higher number of adenomas and FNH included in benign lesion group, suggesting that inclusion of these lesions might have significantly increased the mean SWV.

The cutoff SWV values proposed by the previous studies and accuracies were compared in Table 11, which ranged between 1.82 and 2.73 m/s. The cutoff value from ROC was 1.91 m/s for differentiation of benign and malignant lesions. The cutoff of 2.0 m/s, as proposed by previous studies, revealed fair degree of accuracy with higher positive and negative predictive values and can be recommended for differentiation of benign and malignant or metastatic lesions.

This study has several limitations. First, benign hepatic lesions such as FNH were not included, while few heterogeneous metastatic tumors were evaluated. Second, although SWV in surrounding liver was used for quantification of cirrhosis, the degree of chronic liver disease using Child-Pugh classification was not estimated, which might have an effect on visual inspection. Exclusive study of the malignant lesions with varying degree of cirrhosis in surrounding liver is necessary to establish the true effect of background

Table 10: Comparison of mean shear wave velocities in various groups of lesions in present study with previous studies

Study	Number of lesions evaluated	Mean SWVs in various groups of lesions (m/s)			
		Benign	Malignant	Metastases	*P*
Cho et al., 2010[26]	36	1.51±0.71	2.45±0.81	2.18±0.96	0.012
Kim et al., 2013[27]	101	1.80±0.57	2.66±0.94	2.82±0.97	<0.05
Park et al., 2013[14]	47	1.51±0.69	2.31±1.05	2.35±1.18	0.047
Davies and Koenen et al., 2011[15]	99	1.35±0.48	-	4.23±0.59	<0.0001
Shuang-Ming et al., 2011[16]	128	1.47±0.53	3.16±0.80	-	<0.05
Guo et al., 2015[17]	134	1.69±0.89	2.95±1.00	-	<0.001
Zhang et al., 2013[18]	154	1.33±0.38	2.59±0.91	3.20±0.62	<0.001
Frulio et al., 2013[19]	79	2.53±0.83	2.40±1.01	3.0±1.36	>0.05
Sendroiu et al., 2011[20]	70	1.88±0.99	2.24±0.97	2.48±1.06	0.27
This study	60	1.30±0.35	2.93±0.75	2.77±0.90	<0.0001

SWVs: Shear wave velocities

Table 11: Comparison of proposed cutoff for shear wave velocity values and accuracies in various studies for differentiation of benign and malignant lesions

Study	Number of lesions	SWV (m/s)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	*P*
Cho et al., 2010[26]	36	2.0	74	82	89	60	<0.05
Kim et al., 2013[27]	101	2.73	96.4	76.6	-	-	<0.05
Park et al., 2013[14]	47	1.82	71.8	75	-	-	<0.001
Davies and Koenen et al., 2011[15]	99	2.5	97.1	100	-	-	-
Shuang-Ming et al., 2011[16]	128	2.22	89.7	95	89.7	95	<0.001
Guo et al., 2015[17]	134	2.13	83.3	78	-	-	<0.001
Zhang et al., 2013[18]	154	2.22	81.3	93	-	-	-
Kapoor et al., 2011[21]	42	2.0	94	70	70	94	<0.0001
Yu and Wilson, 2011[22]	105	1.9	61	69	46	80	<0.01
Goya et al., 2015[23]	117	2.52	97	66	-	-	<0.01
This study	60	2.0	92	96	96	93	<0.0001

SWV: Shear wave velocity measured in m/s, PPV: Positive predictive value, NPV: Negative predictive values

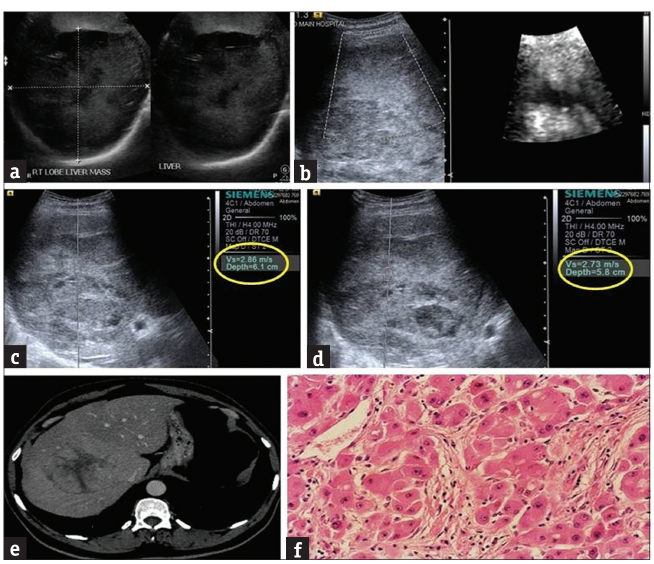

Figure 7: A 59-year-old alcoholic male is with a heteroechoic lesion with central scar on ultrasonography in noncirrhotic liver (a). Elastography reveals that the central scar is much stiffer than the rest of the lesion (b). The lesion appears to be of similar in size as that of B-mode image. Acoustic radiation force impulse elastometry reveals mean shear wave velocity of 2.74 m/s in the lesion (c and d). Contrast-enhanced computed tomography scan showing that the lesion enhances while the central scar does not (e). Postsurgical histopathology revealed fibrolamellar carcinoma showing cords of neoplastic cells separated by lamellar fibrotic strands (f).

cirrhosis on the appearance of lesions in elastography images. Since the degree of fibrosis, cellularity, amount of necrosis, and other parameters contribute to stiffness in imaging, correlation with pathological findings is essential for better understanding of these findings. Although multiple measurements from the lesions improve accuracy, the inter- and intra-observer reproducibility of these findings was not evaluated in detail in this study.

Conclusion

ARFI elastography with ARFI 2D imaging and ARFI quantification (SWVs) can provide valuable additional information to ultrasonography and can significantly improve its ability in characterizing the liver tumors. Although ARFI quantification (SWVs) is a more objective method, information provided in 2D imaging might improve the understanding and accuracy of quantification techniques.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

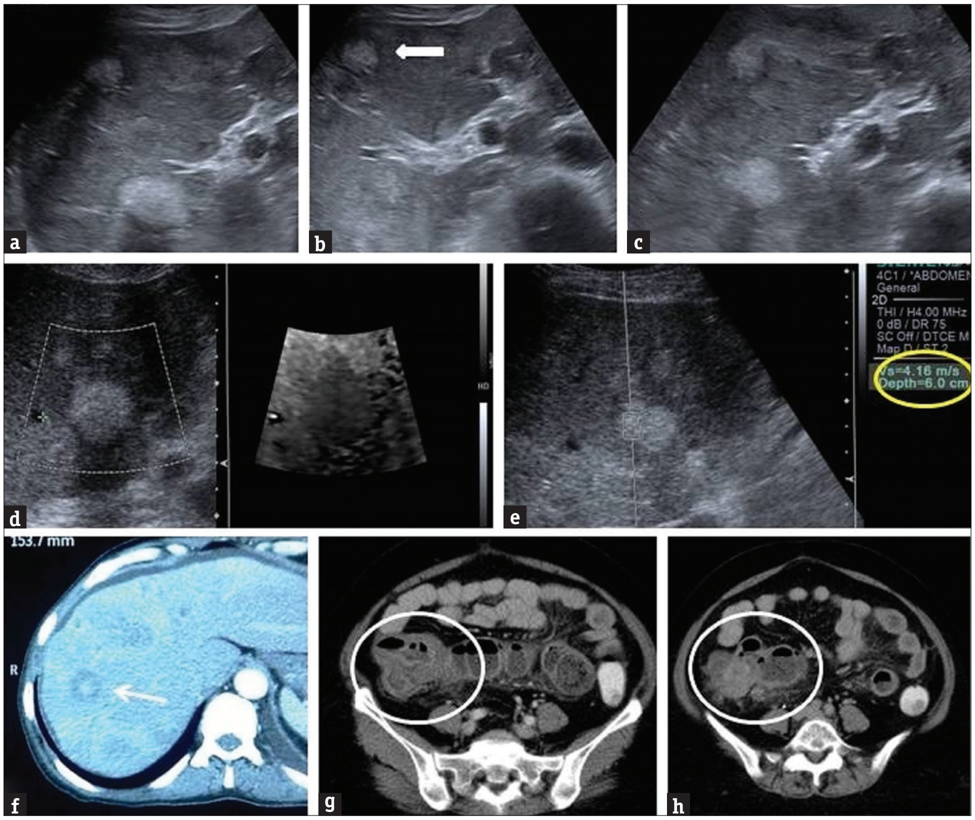

Figure 8: Ultrasonography in 60 yr old male patient showing multiple well defined hyperechoic lesions in both lobes of liver, with some of them showing a thin hypoechoic rim (thick white arrow) (a-c). ARFI elastography reveals that the lesions are stiffer than surrounding liver and larger in size in relation to B-mode image (d). The mean shearwave velocity in the lesion is 3.94 m/s (e). Contrast enhanced CT scan showed a adenocarcinoma of caecum and proximal ascending colon (white circle) with multiple liver secondaries (thin white arrow) (f-h).

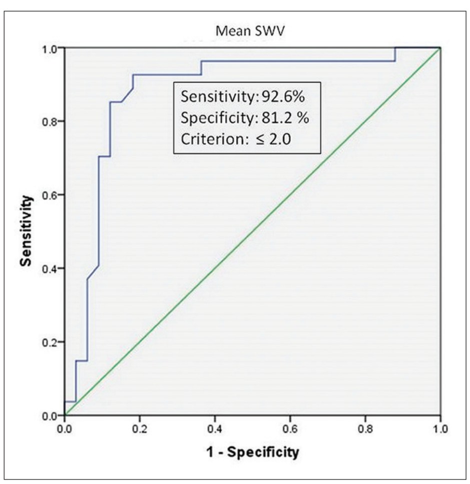

Figure 9: Receiver operating characteristic curve of mean shear wave velocities for differentiation of benign and malignant hepatic lesions.

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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