Application of Real Time Elastography for Assessment of Different Hepatic Focal Lesions

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Abstract

Ultrasound is often the first technique used for the detection and characterisation of focal liver lesions because of its availability, low cost and safety. Shockingly, the affectability and particularity of regular ultrasound is under 70 % for the recognition and characterisation of central liver injuries (FLLs). assess the job of ongoing elastography ultrasound method in portrayal of various HFLS. This is an imminent report, The patients were isolated reflectively into three gatherings: Group 1: included 148 patients who were analyzed as essential harm including hepatocellular carcinoma (HCC) and chlolangiocarcinoma. Gathering 2: included 23 patients who were analyzed as kind injuries, for example, hemangioma, sores and FNH. Gathering 3: included 29 patients who analyzed as metastatic sores, patients were exposed to full history taking, total clinical assessment, lab examinations and imaging as Abdominal ultrasonography, Triphasic CT check ; Dynamic MRI with dissemination; and US guided biopsy and histopathology assessment. The present examination was directed on 200 patients with central liver sores, There was a profoundly factually critical distinction (P-esteem < 0.001) between essential harmful gathering and generous injuries bunch as respect SWE of central injury, SWE of liver and FL/liver proportion. Exceptionally factually noteworthy distinction (P-esteem < 0.001) between essential harmful and metastatic gatherings as respect SWE of central sore and FL/liver proportion. SWE had the option to separate the essential danger from amiable injuries and metastases, as there was exceptionally factually huge distinction as respect SWE perusing of FL/liver proportion (P value<0.001).

Keywords: Real Time Elastography, Hepatic, Focal Lesions.

1. Introduction

Hepatic central injuries (HFLs) are regularly characterized based on appearance into cystic or strong. They can likewise be grouped dependent on the threatening potential into kindhearted or dangerous. Also, when, threatening, they can be grouped dependent on beginning of the malignant cells into essential or metastatic. The differential conclusion of HFLs incorporates amiable sores (eg, hemangioma, central nodular hyperplasia, adenoma, central regenerative hyperplasia, straightforward hepatic growths, polycystic liver illness, bile ductular cystadenoma, and bile ductular hamartomas) and dangerous injuries (eg, essential hepatocellular carcinoma, cholangiocarcinoma, metastatic tumors and lymphoma [1].

Ultrasound is frequently the primary method utilized for the location and portrayal of HFLs on account of its accessibility, ease and wellbeing. Tragically, the explicitness of regular ultrasound is under 70 % for the recognition and portrayal of HFLs [2]. Registered tomography offers the best spatial goals and the capacity to contemplate the whole liver in a solitary breath-hold. It fills in as a perfect screening assessment for the whole stomach area and pelvis. Mechanical advances in CT innovation, for example, helical CT and multidetector helical CT have additionally improved the presentation of CT scanners as far as speed of securing, goals, and the capacity to picture the liver during different periods of difference upgrade more accurately than was conceivable already [3]. Attractive Resonance Imaging has risen as the best imaging test for HFLs location and portrayal, since this methodology gives high sore to-liver differentiation and doesn't utilize ionizing radiation. Advances in MRI, including breath-hold 3D imaging and fast half-Fourier procurement, help picture the liver in a solitary breath-hold with a high spatial goals [4].

Percutaneous biopsy is typically utilized if there is still vulnerability in the wake of imaging; be that as it may, a liver biopsy has the disadvantages of patient uneasiness, agony and dangers of horribleness [5].

A methodology has showed up, that creates shear waves at a point of convergence in the tissue, where the speed of the wave gives a gauge of tissue firmness. Three unique usage of the shear wave procedure have permitted clinical use in the liver. The first is transient elastography (TE), which is utilized for the assessment of fibrosis in the liver and to appraise the firmness of HFLs . In any case, TE gives no imaging segment to direction and the gauge of versatility is thought to be uniform over a 4-cm A-line procurement [6].

The second is acoustic radiation power motivation (ARFI) which is another shear wave-based strategy that gives an increasingly nearby quantitative gauge of versatility, ARFI gives imaging direction to choose wanted locales of tissue for firmness estimation,however this solidness estimation is constrained to a solitary point and single securing. Like TE, ARFI has been applied to HFLs, however it endures a similar constraint of just giving a normal firmness esteem over a fixed district of intrigue $(0.4 \times 0.5$ cm) [7].

The third technique is continuous elastography (RTE) which is additionally coupled to be an analytic framework, yet has the benefit of giving a constant 2D quantifiable picture of tissue firmness, with this strategy, the spatial variety of versatility can be envisioned and enrolled to a B-mode picture, flexibility esteems in the area of intrigue are mapped as a shading show. A few highlights can be portrayed with this procedure, remembering quantitative assessment of the sore versatility for kPa or m/s, the spatial heterogenecity of firmness, and the estimation of the proportion of solidness between the sore and the liver [8].

This investigation intended to assess the job of continuous elastography ultrasound procedure in portrayal of various HFLS.

2. Patients and methods

This is a prospective study, was conducted on 200 patients with focal liver lesions. They were recruited during the period from september 2017 to May 2019. Patients were recruited from the the Gatroenterology and Hepatology department at National Hepatology and Tropical Medicine Research Institute(NHTMRI),. They were divided retrospectively into three groups:

Group 1: included 148 patients who were diagnosed as primary malignancy including hepatocellular carcinoma (HCC) and chlolangiocarcinoma.

Group 2: included 23 patients who were diagnosed as benign lesions such as hemangioma, cysts and FNH.

Group 3: included 29 patients who diagnosed as metastatic lesions such as cancer colon, cancer stomach, GIST, Lymphoma, Cancer pancrease, Cancer breast and suprarenal gland carcinoma.

The study protocol was approved by the scientific committee of Benha faculty of medicine and the Institutional Review Board (IRB) of National Hepatology and Tropical Medicine Research Institute (NHTMRI); Cairo. An informed written consent was obtained from all patients participated in this study after explaining the study measures in details.

Inclusion criteria

- Adult patients > 18 years.
- Right hepatic focal lesions that was well visualized on conventional US.

Exclusion criteria

- Lesions in left hepatic lobe (oscillation of the left liver by cardiac activity may interfere with stiffness measurements).
- Lesions deeper than 8 cm.
- Patient who can't hold his breath for 5 seconds..
- Obstructive Jaundice.
- (ALT) values > 5 folds of upper limit.

- Tense Ascites
- Pregnancy.
- Congestive heart failure.

The selected patients were subjected to full history taking, complete clinical examination, laboratory investigations as complete blood count, kidney function tests, liver function tests, Hepatitis C virus antibody, Hepatitis B virus surface antigen (HBsAg), Tumor markers for metastatic lesions e.g CEA,CA19.9,CA15.3 and B2 microglobulin, AFP (ng/dl) level for HCC, and imaging as Abdominal ultrasonography, Triphasic CT scan ; Dynamic MRI with diffusion; and US guided biopsy and histopathology examination.

2.1 Statistical analysis

The gathered information were organized and broke down utilizing SPSS form 16 delicate product (SpssInc, Chicago, ILL Company. Straight out information were introduced as number and rates. Chi square test (X2), or Fisher's precise test (FET) were utilized to investigate them. Quantitative information were tried for typicality utilizing Kolmogorov Smirniv test, expecting ordinariness at P>0.05. they were introduced as mean±SD if ordinarily circulated, utilizing ANOVA test to evaluate contrasts among ≥3 free methods.. While non parametric factors were introduced as middle and extend and broke down by Kruskal Wallis test (KW). Huge ANOVA and KW tests were trailed by post hoc different correlations utilizing Bonferroni tests to recognize the huge sets. ROC bends were built to identify cutoff estimations of RTE to separate FL of liver. The acknowledged degree of criticalness in this work was expressed at 0.05 (P <0.05 was viewed as noteworthy).

3. Results

The current study was conducted on 200 patients with focal liver lesions, there was highly statistically significant difference (P-value < 0.001) between primary malignant and metastatic groups in comparison to benign lesions group as regard age. Table (1), triphasic CT or MRI findings among the studied groups in Fig (1).

Table (1) Socio-demographic characters of the studied sample.

Variable		Primary malignancy (n=148)		Benign lesions (n=23)		Metastatic (n=29)		ANOVA	P
Age (ys)	Mean±SD	57.2±7.4*		47.1±10.9		55.5±8.9*		15.6	<0.001 (HS)
	Range	37-78		26-68		33-67			
		No.	%	No.	%	No.	%	χ^2 test	P
Sex	Male	120	81.1	17	73.9	14	48.3	14.1	0.001
	Female	28	18.9	6	26.1	15	51.7		(S)
Residence	Rural	117	79.1	15	65.2	16	55.1	13.8	0.001
	Urban	31	20.9	8	34.8	13	44.9		(S)
Smoking	Smoker	110	74.3	14	60.8	15	51.7	13.4	0.001
	Non smoker	38	25.7	9	39.2	14	48.3		(S)

*→Significance in comparison with benign lesions
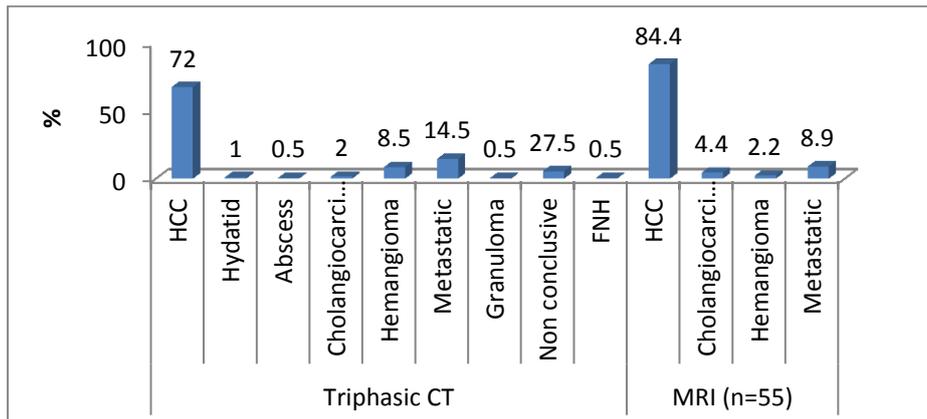HS: P-value < 0.001 is considered highly significant.

Fig (1) Bar chart showing triphasic CT or MRI findings among the studied groups.

There is a statistically significant difference (P-value < 0.05) between primary malignant group in comparison to metastatic and benign groups as regard jaundice, bleeding tendency, hepatic encephalopathy, ascites and splenomegaly, Table (2).

Table (2) Comparison between studied groups as regard medical history and clinical findings.

Variables no (%)	Primary malignancy No = 148	Benign lesions no=23	Metastatic lesions no=29	Statistical test (X2)	P-value
DM	50 (33.8)	5 (21.8)	10 (34.5)	0.13	>0.05
HTN	40 (26)	3 (13.1)	8 (27.6)	0.04	>0.05
Jaundice	87 (58.8) *	2 (8.7)	9 (31)	1.4	<0.05
Hepatic encephalopathy	7 (4.8) *	0 (0)	0 (0)	1.7	<0.05
Bleeding tendency	46 (31.1) *	0 (0)	4 (13.8)	1.1	<0.05
Hepatomegaly	14 (9.5)	4 (17.4)	9 (31)	0.3	>0.05
Splenomegaly	125 (84.5) *	3 (13)	11 (38)	2.4	<0.05
Ascites	17 (11.5) *	0 (0)	1 (3.5)	1.3	<0.05
Weight loss	53 (35.9)	6 (26)	20 (69)	0.5	>0.05

*→Significance in comparison with metastatic and benign lesions.

The histopathological examination of some hepatic focal lesions which not diagnosed by imaging, in Fig (2).
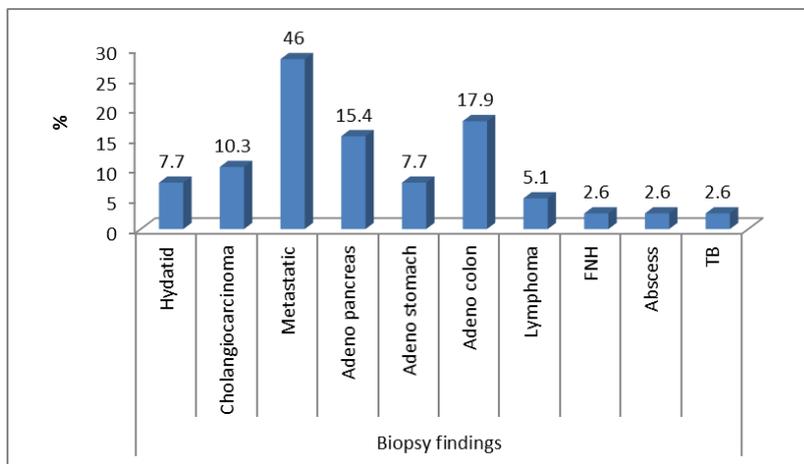4R

Fig (2) The histopathological examination of some hepatic focal lesions which not diagnosed by imaging.

There was a highly statistically significant difference (P-value > 0.001) between primary malignant and metastatic groups in comparison to benign lesions group as regard H.b and, Creat. Highly statistically significant difference (P-value < 0.001) between primary malignant group in comparison to benign lesions group and metastatic groups as regard Platelets. Highly statistically significant difference (P-value < 0.001) between primary malignant group in comparison to metastatic groups as regard AFP. statistical significant difference (P-value < 0.05) between primary malignant group in comparison to metastatic groups as regard TLC. Highly statistically significant difference (P-value < 0.001) between primary malignant and metastatic groups in comparison to benign lesions group as regard ALT, AST, INR, Albumin and Bilirubin. Highly statistically significant difference (P-value < 0.001) between primary malignant and metastatic groups as regard Albumin and INR Table (3).

Table (3) Comparing the laboratory findings among the studied groups.

Variable	Primary malignancy (n=148)		Benign lesions (n=23)		Metastatic (n=29)		+-*	P
	Median	Range	Median	Range	Median	Range		
TLC	10.0†	2.3-18	7.6†	4.1-14	12.0	5.1-15.4	9.8	0.007 (S)
Hb	10.0*	7.4-15	13.0	10-15	10.4*	7.5-13.2	45.08	<0.001 (HS)
PLTs	104.0*†	34-311	312.0	188-501	345.0	111-567	101.8	<0.001 (HS)
RBS	188.5	77-401	154.0	95-321	195.0*	102-354	6.5	0.039 (S)
Creat	1.1*	0.6-2.3	0.8	0.5-1.1	1.1*	0.5-2.1	19.9	<0.001 (HS)
AFP	73.9†	3.4-2601	45.0	2.6-55	12.3	2.3-76	36.03	<0.001 (HS)
ALT	76*	19-213	45	12-99	88*	45-345	20.8	<0.001 (HS)
AST	55*	12-211	29	12-76	65*	11-233	16.5	<0.001 (HS)
Bilirubin	1.7*	0.9-18	0.9	0.4-1.5	1.3*	0.9-15.4	64.9	<0.001 (HS)
Albumin	3.2*†	2.4-3.9	3.7	3.1-4.5	3.5*	3.1-4.2	63.1	<0.001 (HS)
INR	1.6*†	1.1-2.3	1.1	0.9-1.4	1.3*	0.9-1.9	85.6	<0.001 (HS)

*→Significance in comparison with benign lesions
†→ Significance in comparison with metastatic lesions
HS: P-value < 0.001 is considered highly significant.
S: P-value ≤ 0.05 is considered significant.

There was a highly statistically significant difference (P-value < 0.001) between primary malignant group and benign lesions group as regard SWE of focal lesion,SWE of liver and FL/liver ratio. Highly statistically significant difference (P-value < 0.001) between primary malignant and metastatic groups as regard SWE of focal lesion and FL/liver ratio Table (4).

Table (4) Comparing the studied groups regarding SWE.

Variable	Primary malignancy (n=148)		Benign lesions (n=23)		Metastatic (n=29)		KW test	P
	Median	Range	Median	Range	Median	Range		
SWE of FL	6.1*	1.98-14.3	4.4	1.4-10.8	5.3	1.3-9.5	15.9	<0.001 (HS)
SWE of liver	19.3*†	3.15-41.3	7.4	3.7-14.1	10.4	4.06-18.3	99.2	<0.001 (HS)
FL/liver ratio	0.336*†	0.09-1.64	0.576	0.11-1.3	0.506	0.07-1.31	36.1	<0.001 (HS)

*→Significance in comparison with benign lesions
†→ Significance in comparison with metastatic lesions.
HS: P-value < 0.001 is considered highly significant.

There is significant difference in stiffness between HCC and Cystic lesions, HCC and hemangioma and between HCC and FNH. No significant difference was observed in lesions' stiffness between HC and cholangiocarcinoma and between HCC and metastasis. The table also shows significantly higher liver parenchyma stiffness in HCC when compared to liver parenchyma in the other studied hepatic focal lesions Table (5).

Table (5) Characterization of various lesions on their appearance on stiffness by SWE in relation to the surrounding liver parenchyma.

Stiffness of lesions	Primary malignancy No= 148	Benign lesions no =23	Metastatic lesions no = 29
Stiffer	HCC (1) CC(0)	Hemangioma (1) FNH (1)	Cancer stomach (1) Lymphoma (2)
Similar stiffness	HCC (1) CC (0)	Hemangioma (4) Hydatid cyst (1)	Cancer colon (2)
Softer	HCC (142) CC (4)	Hemangioma (12) Hydatid cyst (2) T.B (1) Pyogenic Abscess (1)	Cancer breast (6) Cancer pancreas (6) Cancer colon (5) Cancer stomach (2) GIST (2) Cancer gall bladder (1) Cancer suprarenal gland (2)

The stiffness of lesions by SWE were described in Table (6).

Table (6) Characterization of various lesions on their appearance on stiffness by SWE in relation to the surrounding liver parenchyma.

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Softer	HCC (142) CC (4)	Hemangioma (12) Hydatid cyst (2) T.B (1) Pyogenic Abscess (1)	Cancer breast (6) Cancer pancreas (6) Cancer colon (5) Cancer stomach (2) GIST (2) Cancer gall bladder (1) Cancer suprarenal gland (2)

ROC curve analysis showed SWE FL$\geq$5.36, SWE liver $\geq$13.3 and SWE $\leq$0.444 ratio can significantly differentiate FL of primary malignancies from other lesions, Fig (3).
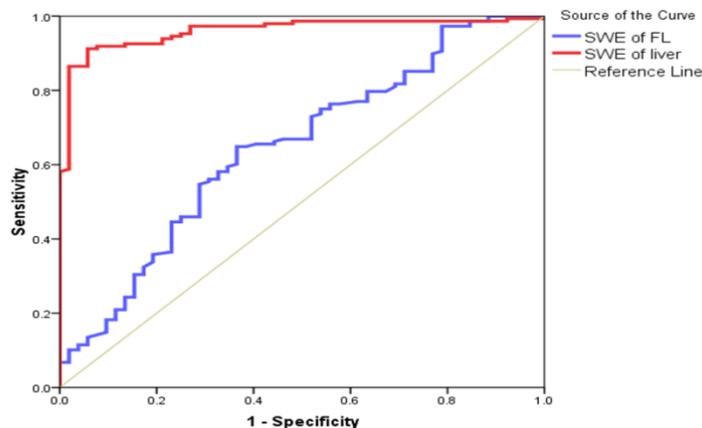

Fig (3) ROC curve analysis of SWE of FL and liver

4. Discussion

The mean period of essential threat patients was 57 ± 2 year, these discoveries go in concurrence with [9], who revealed that the mean time of HCC is 57 ± 9.

In the favorable sores gathering, the vast majority of the patients (73.9%) were guys; their mean age was 47.1 ± 10.9 years old. these discoveries go in opposite with [10], whom announced that ladies are influenced more regularly than men. The female-to-male proportion is 5:1& hepatic hemangiomas can happen at various ages, however for the most part analyzed in people matured in the middle of 33-48 years.

In the metastatic gathering, (55 %) of the patients were females and (45 %) were guys. These discoveries go in opposite with [11] Who revealed that recurrence of liver metastases was higher in guys (18.2%) than in females (13.4%) from patients with colorectal malignancy.

The mean hemoglobin level was higher in the metastases patients in examination with HCC patients. Our outcomes were in opposite with [12], whom detailed that hemoglobin in HCC is higher than metastatic due to Paraneoplastic erythrocytosis that happen because of expanded tumor erythropoietin created by the HCC.

The middle platelets include was essentially lower in the essential dangerous gathering contrasted with the metastasis gathering (p<0.001), and to the generous sores gathering (p<0.001). Our outcomes were in concurrence with [13], whom announced that the danger of creating HCC increments continuously in male patients, with cutting edge age, low platelet check, and esophageal varices

Essential dangerous and metastatic patients demonstrated critical rise in ALT, AST and serum Bilirubin levels in contrast with kind sores. Our outcomes were in concurrence with [14].

In this examination, there is no measurably critical distinction between solidness in kind sores and the encompassing liver tissue. On the in spite of [7], portrayed that kindhearted injuries particularly hemangiomas have marginally raised solidness contrasted and the encompassing liver [15], clarified this rise in firmness because of the nearness of sinewy septae isolating the blood occupied spaces.

If there should arise an occurrence of FNH, it was more enthusiastically than the encompassing liver tissue, demonstrating mean versatility estimation of (10.8) kpa, while the mean flexibility estimation of the encompassing liver parenchyma was (8.2) kpa. This can be clarified with the notable high fibrotic substance of this kind of sore.

Our outcome goes in concurrence with [16], whom saw that FNH showed up as the "hardest" kindhearted tumor.

There is distinction in firmness between metastatic central injuries (5.3 Kpa) and the foundation hepatic tissue (10.4 kpa) with (p esteem < 0.001) .This finding was on the in spite of [7], [16], whose reviews revealed that metastatic central sores had the most elevated SWE values.

At that point we expected to analyze solidness of central injuries between the contemplated gatherings.

SWE had the option to separate between essential harm and favorable sores, as there was measurably critical contrast between SWE perusing of the two gatherings (P esteem < 0.001). Our outcomes were in concurrence with [17], who revealed that solidness of HCC was essentially higher than that of the kindhearted sores particularly hemangioma.

SWE couldn't separate between hepatic metastases and essential harm, as there was no factually critical distinction between the two gatherings (P value= 0.2). This finding goes in concurrence with [18], who revealed that the distinction in the flexibility esteems among HCC and liver metastasis bunches were not measurably huge. on the as opposed to [19], who revealed that firmness of HCC was fundamentally higher than that of the metastasis.

5. Conclusion

SWE was able to differentiate the primary malignancy from benign lesions and metastases, as there was highly statistically significant difference as regard SWE reading of FL/liver ratio (P value<0.001).

References

[1] O. Shaked, E. S. Siegelman, K. Olthoff, "Biologic and clinical features of benign solid and cystic lesions of the liver," Clin. Gastroenterol. Hepatol., Vol. 9, 7, PP. 547–562, 2011.

[2] K. Wernecke, "Detection of hepatic masses in patients with carcinoma: comparative sensitivities of sonography, CT, and MR imaging.," AJR. Am. J. Roentgenol., Vol. 157, PP. 731–739, 1991.

[3] R. de Franchis, "Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension," J. Hepatol., Vol. 53, PP. 762–768, 2010.

[4] S. J. Hahn, J. Park, J. H. Lee, "Severe hypertriglyceridemia in diabetic ketoacidosis accompanied by acute pancreatitis: case report," J. Korean Med. Sci., Vol. 25, PP. 1375–1378, 2010.

[5] W.-C. Yeh, "Elastic modulus measurements of human liver and correlation with pathology," Ultrasound Med. Biol., Vol. 28, PP. 467–474, 2002.

[6] R. Masuzaki., "Assessing liver tumor stiffness by transient elastography," Hepatol. Int., Vol. 1, PP. 394–397, 2007.

[7] R. Heide, D. Strobel, T. Bernatik, "Characterization of focal liver lesions (FLL) with acoustic radiation force impulse (ARFI) elastometry," Ultraschall der Medizin-European J. Ultrasound, Vol. 31, PP. 405–409, 2010.

[8] D. O. Cosgrove., "Shear wave elastography for breast masses is highly reproducible," Eur. Radiol., Vol. 22, PP. 1023–1032, 2012.

[9] J. Collier and M. Sherman, "Screening for hepatocellular carcinoma," Hepatology, Vol. 27, PP. 273–278, 1998.

[10] H.-J. Kwon , "Acoustic radiation force impulse elastography for hepatocellular carcinoma-associated radiofrequency ablation," World J. Gastroenterol.

WJG, Vol. 17, PP.1-874, 2011.

[11] G. I. Nedredal, "Portal hypertension correlates with splenic stiffness as measured with MR elastography," J. Magn. Reson. Imaging, Vol. 34, PP. 79–87, 2011.

[12] F. Pons, M. Varela, J. M. Llovet, "Staging systems in hepatocellular carcinoma," Hpb, Vol. 7, PP. 35–41, 2005.

[13] A. S. Lok "Incidence of hepatocellular carcinoma and associated risk factors in hepatitis C-related advanced liver disease," Gastroenterology, Vol. 136, PP. 138–148, 2009.

[14] T. Akatsu, G. Wakabayashi, A. Tanimoto, K. Kameyama, and M. Kitajima, "Inflammatory pseudotumor of the liver masquerading as hepatocellular carcinoma after a hepatitis B virus infection: report of a case," Surg. Today, Vol. 36, PP. 1028–1031, 2006.

[15] A. Guibal et al., "Evaluation of shearwave elastography for the characterisation of focal liver lesions on ultrasound," Eur. Radiol., Vol. 23, PP. 1138–1149, 2013.

[16] N. Frulio ,Evaluation of liver tumors using acoustic radiation force impulse elastography and correlation with histologic data," J. ultrasound Med., Vol. 32, PP. 121–130, 2013.

[17] H. S. Park, Y. J. Kim, M. H. Yu, S. Il Jung, and H. J. Jeon, "Shear wave elastography of focal liver lesion: intraobserver reproducibility and elasticity characterization," Ultrasound Q., Vol. 31, PP. 262–271, 2015.

[18] S.Bota,"The influence of aminotransferase levels on liver stiffness assessed by Acoustic Radiation Force Impulse Elastography: a retrospective multicentre study," Dig. Liver Dis., Vol. 45, PP. 762–768, 2013.

[19] J. Bruix and M. Sherman, "AASLD practice guideline," Manag. Hepatocell. carcinoma. Hepatol., Vol. 42, PP. 1208–1236, 2005.