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Ultrasound Shear Wave Elastography in the Evaluation of Liver Fibrosis

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Abstract

Background: Chronic hepatitis B virus (HBV) infection affects about 296 million people worldwide and is the leading etiology of cirrhosis and liver cancer globally. In China, chronic hepatitis B has grown to be a significant public health issue. NAFLD (non-alcoholic fatty liver disease) is one of the primary causes of cirrhosis in the globe. Up to 10.3% of NAFLD patients, according to the National Health and Nutrition Examination Survey, had advanced fibrosis. These findings suggest that the real-time Shear wave elastography (SWE) can be used for the assessment of significant fibrosis, sever fibrosis and Cirrhosis. Objective: To determine the ultrasound shear wave elastography in the evaluation of liver fibrosis. Methods: A cross-sectional study was conducted at First affiliated hospital of Xinjiang Medical university, which was performed between January 2020 and March 2023. The total patients in our study was 118. In 118 consecutive patients who underwent Ultrasound Shear wave elastography (SWE) before their scheduled liver biopsy (59 men, 59 women). We used Michael Mindray ultrasound machine and its frequency was C6-1. The stages of liver fibrosis according to the METAVIR classification system. Results: F2 stage of fibrosis is more as compare as compare to others. Liver fibrosis is more common in females as comapre to males. According to the age males have higher risk as compare to females. Total patients in our study was 118. Mean age for males patienst were 44.8983 and for females 48.9492. MEAN±SD of Alanine aminotransferase (ALT) was 92.6±116.14 u/L. The frequency of patients with F0 was 33 (28.0 %), F1 was 5 (4.2%), F2 was 58 (49.2%), F3 was 9 (7.6%) F4 was 13 (11.0%). Frequency of no fatty liver was 49, mild fatty liver was 39, moderate fatty liver was 8, sever fatty liver was 22. Hepatitis B was present in 96 patients and was not present in 22 patients out of 118. Hepatitis C was present in 116 patients and was not present in 2 patients out of 118 (1.7). P-value of hepatitis B is 0.34. P-value of hepatitis C is 1.0. P-value of stages of Liver fibrosis with respect to gender is 0.005. Conclusion: Our result concluded that fibrosis stage F2 patients are more in our study (Heaptitis B). Liver fibrosis is more common in females as compare to males. According to the age males have higher risk as compare to females. Shear wave elastography (SWE) is a straightforward, quick, and repeatable technique for noninvasively assessing liver fibrosis. Benefits include its low cost and global availability.

Keywords: Ultrasound Shear Wave Elastography (SWE), Liver Fibrosis, Chronic Hepatitis B Virus (HBV) and Hepatitis C

1. Introduction

Chronic hepatitis B virus (HBV) infection affects about 296 million people worldwide and is the principal etiology of cirrhosis and liver cancer globally (Hsu et al., 2023). In China, chronic hepatitis B has emerged as a major public health issue (Zheng et al., 2020). Liver biopsy is now the gold standard for determining if someone has cirrhosis or liver fibrosis (Karkmann et al., 2018). Between 20 and 30 percent of persons in Western countries have nonalcoholic fatty liver disease (NAFLD) (Vernon et al., 2011). The reference standard for grading steatosis and inflammation, two characteristics unique to steatohepatitis, and staging fibrosis, a measure of the severity of liver disease, is often liver biopsy (Kleiner et al., 2005; Sanyal et al., 2005). However, liver biopsy is an intrusive procedure that comes with risk of bleeding, discomfort, and inaccurate sample (Fernandez et al., 2011; Myers et al., 2008). As a result, a noninvasive method is required for the evaluation of hepatic steatohepatitis. Cirrhosis, cancer, and liver failure can develop from hepatic fibrosis. Depending on the degree of liver fibrosis, many clinical therapy modalities exist (Barr et al., 2020). The creation of elasticity-based ultrasonography (US) methods, which assess the speed of elastic shear waves to offer a quantitative assessment of liver stiffness represents a significant advancement in the noninvasive examination of liver fibrosis (Bamber et al., 2013; Grgurevic et al., 2015). In particular for cirrhosis, it has demonstrated high accuracy in fibrosis detection (Friedrich et al., 2008; Bohte et al., 2014). Elastography can only measure stiffness, despite the fact that liver stiffness is often closely linked with the degree of fibrosis (Goodman 2007). Cirrhotic nodules are one example of a fibrotic formation that can grow to be bigger than the US wavelength (Toyoda et al., 2009). One of the main causes of cirrhosis globally is non-alcoholic fatty liver disease (NAFLD) (Gbd, 2017). NAFLD is one of the leading and fastest-growing causes of chronic liver disease worldwide followed by obesity and insulin resistance (Younossi et al., 2016; Younossi et al., 2018). Up to 10.3% of NAFLD patients had advanced fibrosis, according to the National Health and Nutrition Examination Survey (Le et al., 2017). These results imply that real-time SWE can be utilized to evaluate cirrhosis, severe fibrosis, and substantial fibrosis (Jing et al., 2017).

2. Materials and Methods

A cross-sectional study was conducted at First affiliated hospital of Xinjiang Medical University, which was performed between January 2020 and March 2023, The total patients in our study was 118. In 118 consecutive patients who underwent Ultrasound Shear wave elastography (SWE) before their scheduled liver biopsy (59 men, 59 women). We used Michael Mindray ultrasound machine and its frequency was C6-1. The stages of liver fibrosis according to the METAVIR classification system. Informed consent was obtained from all patients. Shear wave elastography (SWE) measurements were obtained at four sites in the liver. Biopsy specimens were reviewed in a blinded manner by a pathologist using METAVIR criteria. SWE measurements and biopsy results were compared by using the Spearman correlation and receiver operating characteristic (ROC) curve analysis. Data was tabulated and analyzed by SPSS.

2.1. Clinical and laboratory examination

Weight, sex, and age were noted. After the patients had fasted for eight hours, venous blood samples were taken in order to evaluate the enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST), glutamyltranspeptidase (GGT), and alkaline phosphatase (ALP). Body mass index (BMI).

3. Results

According to our study total patients were 118, Distribution of patients according to gender was (59 were males and 59 were females). Distribution of patients according to mean age (out of 118 patients, 44.8983 were males and 48.9492 were females). Distribution of patients according to mean age of standard deviation (16.16 were males and 12.92 were females). Graphical Representation of gender represent that both gender are same in number 59 were males and 59 were females.

Variable	Frequency	Percentage
Gender:		
Male	59	100.0
Female	59	100.0
Total	118	100%
	Mean	SD
Age		
Male	44.8983	16.16
Female	48.9492	12.92
Total Age	46.92	14.71

Table 1: Distribution of patients according to gender and mean age (n=118)



Mean and Standard Deviation (SD) of liver Function

MEAN±SD of Alanine aminotransferase (ALT) was 92.6±116.14 u/L, MEAN±SD of Aspartate aminotransferase (AST) was 74.23±81.75 u/L, MEAN±SD of Alkaline phosphate (ALP) was 302.46±999.9 u/L, MEAN±SD of Total Bilirubin (TBIL) was 55.03±204.98 umol/L, MEAN±SD of bilirubin test (DBIL) was 7.28±21.3 umol/L, MEAN±SD of Gamma-glutamyl transferase (GGT) was 172.80±711.1 u/L, MEAN±SD of Creatine kinase (CNE) was 4938.51±2287.2 u/L, MEAN±SD of Blood nitrogen urea (BUN) was 43.59±31.5 mmol/L,

Table 2: Mean and SD of enrolled patients (n=118)

Variables MEAN±SD	
ALT	92.6±116.14
AST	74.23±81.75
ALP	302.46±999.9
TBIL	55.03±204.98
DBIL	7.28±21.3
GGT	172.80±711.1
CNE	4938.51±2287.2
BUN	43.59±31.5



The stages of Liver fibrosis according to the METAVIR classification system (n=118), The frequency of patients with F0 was 33 (28.0 %), The frequency of patients with F1 was 5 (4.2%) The frequency of patients with F2 was 58 (49.2%), The frequency of patients with F3 was 9 (7.6%) The frequency of patients with F4 was 13 (11.0%) In the above pie graph F2: 49%, F0: 28%, F4: 11%, F3: 8% and F1: 4%.

Distribution of patients on the basis of Fatty Liver (n=118). Frequency of no fatty liver was 49 and its percentage was 41.5 %. Frequency of mild fatty liver was 39 and its percentage was 33.1 %. Frequency of moderate fatty liver was 8 and its percentage was 6.8 %. Frequency of sever fatty liver was 22 and its percentage was 18.6 %.

Table 3: Distribution of patients on the basis of Fatty Liver $(n=118)$

Fatty liver	Frequency	Percentage
No	49	41.5
Mild	39	33.1
Moderate	8	6.8
Severe	22	18.6
Total	118	100.0

Table 3: The mean BMI of enrolled patients (n=118)

BMI

24.10±4.28



the liver area (Significant Fibrosis)

Distribution of patients on the basis of Hepatitis B and Hepatitis C with respect to gender (n=118). Hepatitis B was present in male patients 58 (98.3%) and Hepatitis B was not present in male patients 1 (1.7%). Hepatitis B was present in female patients 58 (98.3%) and Hepatitis B was not present in female patients 1 (1.7%). P-value of hepatitis B is 0.34.

Hepatitis C was present in male patients 46 (78.0%) and Hepatitis C was not present in male patients 13 (22.0%). Hepatitis C was present in female patients 50 (84.7%) and Hepatitis C was not present in female patients 9 (15.3%).

P-value of hepatitis C is 1.0

Distribution of patients on the basis of hepatitis B and hepatitis C (n=118)

Hepatitis B was present in 96 patients out of 118 (81.4%), Hepatitis B was not present in 22 patients out of 118 (18.6). Hepatitis C was present in 116 patients out of 118 (98.3%), Hepatitis C was not present in 2 patients out of 118 (1.7).

Table 4: Distribution of patients on the basis of Hep B and Hep C with respect to gender (n=118)

		Hepatitis B	
Gender	Frequency	Percentage	P-Value
MALE			
YES	58	98.3	_
NO	1	1.7	- 0.34
FEMALE			- Not
YES	58	98.3	- significant
NO	1	1.7	_
	Hepatitis C		
Male			
YES	46	78.0	_
NO	13	22.0	- 1.0
Female			- Not
YES	50	84.7	_ 515milleant
NO	9	15.3	_



Distribution of patients on the basis of Stages of Liver fibrosis with respect to gender (n=118). Frequency of F0 in male Patients was 25 (42.4%), Frequency of F1 in male Patients was 1 (1.7%), Frequency of F2 in male Patients was 26 (44.1%), Frequency of F3 in male Patients was 2 (3.4%), Frequency of F4 in male Patients was 5 (8.5%). Frequency of F0 in female Patients was 8 (13.6%), Frequency of F1 in female Patients was 7 (11.9%), Frequency of F4 in female Patients was 8 (13.6%).

Table 5: Distribution of patients on the basis of Stages of fibrosis with respect to gender (n=118)

		Stages of fibrosis	
Gender	Frequency	Percentage	P-Value
MALE			_
FO	25	42.4	
F1	1	1.7	
F2	26	44.1	-
F3	2	3.4	-
F4	5	8.5	
FEMALE			- 0.005
FO	8	13.6	- significant
F1	4	6.8	•
F2	32	54.2	_
F3	7	11.9	•
F4	8	13.6	



F4: Cirrhosis or advanced scarring

97



Figure 6: Pie Graph Representation of Stages of Fibrosis

P-value of stages of Liver fibrosis with respect to gender is 0.005.

4. Discussion

In this study, the diagnostic precision of real-time Shear wave elastography (SWE) in estimating liver fibrosis was compared against histology. These findings suggest that real-time SWE can be used for the assessment of significantfibrosis, severe fibrosis, and cirrhosis (Jing et al., 2017). Currently, the pathological evaluation of hepatic wound tissue is still required for the diagnosis of liver fibrosis. The approach is intrusive, hence its widespread usage in clinical practice is currently restricted. The development of a non-invasive diagnostic indicator for liver fibrosis has received a lot of attention (Lu et al., 2003). In this prospective cross-sectional study, we evaluated the ideal region from which to obtain measurements and estimated the diagnostic accuracy of SWE for liver fibrosis estimation in patients with chronic liver disease CLD and hepatitis C virus HCV using liver biopsy as the standard of reference (Samir et al., 2015). In clinical practice, the precise and non-invasive categorization of liver fibrosis is of utmost importance. Recently, a deep learning system for employing ultrasound shear wave elastography to stage liver fibrosis was published, and it performed well (Yasaka et al., 2018). Histopathologically, hepatic fibrosis is a consequence of the excessive accumulation of extracellular matrix components in the liver. This process is caused by a wound healing response to persistent liver damage, inducing hepatic stellate cell activation, high alpha smooth muscle actin production, and collagen type I and III secretion, and can progress to cirrhosis (Crespo et al., 2016). Liver fibrosis results from excessive extracellular matrix accumulation due to injury and main to cirrhosis, cancer and death (Ullah et al., 2022). Imaging allows for the assembling of sufficient detailed information on the overall levels of probe accumulation in the tissue or organ of interest due to the much clearer images of the anatomical and spatial distribution of the probe (Tuguntaev et al., 2022).

5. Conclusion

Our result concluded that F2 fibrotic patients are more in our study (Heaptitis B). Liver fibrosis is more common in females as compare to males. According to the age males have higher risk as compare to females. Shear wave elastography (SWE) is a straight forward, quick, and repeatable technique for noninvasively assessing liver fibrosis. Benefits include its low cost and global availability.

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References

- Barr, R. G., Wilson, S. R., Rubens, D., Garcia-Tsao, G., & Ferraioli, G. (2020). Update to the Society of Radiologists in Ultrasound Liver Elastography Consensus Statement. Radiology, 296(2), 263-274. https://doi.org/10.1148/radiol.2020192437
- Bamber, J., Cosgrove, D., Dietrich, C. F., Fromageau, J., Bojunga, J., Calliada, F., Cantisani, V., Correas, J. M., D'Onofrio, M., Drakonaki, E. E., Fink, M., Friedrich-Rust, M., Gilja, O. H., Havre, R. F., Jenssen, C., Klauser, A. S., Ohlinger, R., Saftoiu, A., Schaefer, F., Sporea, I., ... Piscaglia, F. (2013). EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 1: Basic principles and technology. Ultraschall in der Medizin (Stuttgart, Germany 1980), 34(2), : 169–184. https://doi.org/10.1055/s-0033-1335205
- Bohte, A. E., de Niet, A., Jansen, L., Bipat, S., Nederveen, A. J., Verheij, J., Terpstra, V., Sinkus, R., van Nieuwkerk, K. M., de Knegt, R. J., Baak, B. C., Jansen, P. L., Reesink, H. W., & Stoker, J. (2014). Noninvasive evaluation of liver fibrosis: a comparison of ultrasound-based transient elastography and MR elastography in patients with viral hepatitis B and C. European radiology, 24(3), 638–648. https://doi.org/10.1007/s00330-013-3046-0
- Fernández-Salazar, L., Velayos, B., Aller, R., Lozano, F., Garrote, J. A., & González, J. M. (2011). Percutaneous liver biopsy: patients' point of view. Scandinavian journal of gastroenterology, 46(6), 727-731. https://doi.org/10.3109/00365521.2011.558112
- Friedrich-Rust, M., Ong, M. F., Martens, S., Sarrazin, C., Bojunga, J., Zeuzem, S., & Herrmann, E. (2008). Performance of transient elastography for the staging of liver fibrosis: a metaanalysis. Gastroenterology, 134(4), 960-974. https://doi.org/10.1053/j.gastro.2008.01.034
- Grgurevic, I., Puljiz, Z., Brnic, D., Bokun, T., Heinzl, R., Lukic, A., Luksic, B., Kujundzic, M., & Brkljacic, B. (2015). Liver and spleen stiffness and their ratio assessed by real-time two dimensional-shear wave elastography in patients with liver fibrosis and cirrhosis due to chronic viral hepatitis. European radiology, 25(11), 3214-3221.https://doi.org/10.1007/s00330-015-3728x
- Goodman Z. D. (2007). Grading and staging systems for inflammation and fibrosis in chronic liver diseases. Journal of hepatology, 47(4), 598-607. https://doi.org/10.1016/j.jhep.2007.07.006
- GBD 2017 Cirrhosis Collaborators (2020). The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. The lancet. Gastroenterology & hepatology, 5(3), 245-266. https://doi.org/10.1016/S2468-1253(19)30349-8
- Hsu, Y. C., Huang, D. Q., & Nguyen, M. H. (2023). Global burden of hepatitis B virus: current status, missed opportunities and a call for action. Nature reviews. Gastroenterology & hepatology, 20(8), 524-537. https://doi.org/10.1038/s41575-023-00760-9.
- Karkmann, K., Piecha, F., Rünzi, A. C., Schulz, L., von Wulffen, M., Benten, D., Kluwe, J., & Wege, H. (2018). Versorgung bei kompensierter Leberzirrhose 2018 - Evidenzbasierte prophylaktische Maßnahmen [Management of compensated liver cirrhosis 2018 - Evidence based prophylactic measures]. Zeitschrift fur Gastroenterologie, 56(1), 55-69. https://doi.org/10.1055/s-0043-124000
- Kleiner, D. E., Brunt, E. M., Van Natta, M., Behling, C., Contos, M. J., Cummings, O. W., Ferrell, L. D., Liu, Y. C., Torbenson, M. S., Unalp-Arida, A., Yeh, M., McCullough, A. J., Sanyal, A. J., & Nonalcoholic Steatohepatitis Clinical Research Network (2005). Design and validation of a histological scoring system for nonalcoholic fatty disease. *Hepatology* liver (Baltimore, *Md.*), *41*(6), 1313-1321. https://doi.org/10.1002/hep.20701.
- Le, M. H., Devaki, P., Ha, N. B., Jun, D. W., Te, H. S., Cheung, R. C., & Nguyen, M. H. (2017). Prevalence of non-alcoholic fatty liver disease and risk factors for advanced fibrosis and mortality in the United States. PloS one, 12(3), e0173499. https://doi.org/10.1371/journal.pone.0173499
- Liu, J. H., Zou, Y., Chang, W., Wu, J., Zou, Y., Xie, Y. C., Lu, Y. P., & Wei, J. (2017). Assessment of Liver Fibrosis Using Real-time Shear-wave Elastography for Patients with Hepatitis B e Antigen-negative Chronic Hepatitis B and Alanine Transaminase <2 Times the Upper Limit of Normal. Revista de investigacion clinica: organo del *Hospital* de Enfermedades de la Nutricion, 69(5), 254-261. https://doi.org/10.24875/ric.17002215
- Lu, L. G., Zeng, M. D., Wan, M. B., Li, C. Z., Mao, Y. M., Li, J. Q., Qiu, D. K., Cao, A. P., Ye, J., Cai, X., Chen, C. W., Wang, J. Y., Wu, S. M., Zhu, J. S., & Zhou, X. Q. (2003). Grading and staging of hepatic fibrosis, and its relationship with noninvasive diagnostic parameters. World journal of gastroenterology, 9(11), 2574-2578. https://doi.org/10.3748/wjg.v9.i11.2574
- Myers, R. P., Fong, A., & Shaheen, A. A. (2008). Utilization rates, complications and costs of percutaneous liver biopsy: a population-based study including 4275 biopsies. Liver international: official journal of the

International Association for the Study of the Liver, 28(5), 705–712. https://doi.org/10.1111/j.1478-3231.2008.01691.x

- Sanyal, A. J., Brunt, E. M., Kleiner, D. E., Kowdley, K. V., Chalasani, N., Lavine, J. E., Ratziu, V., & McCullough, A. (2011). Endpoints and clinical trial design for nonalcoholic steatohepatitis. *Hepatology (Baltimore, Md.*), 54(1), 344–353. https://doi.org/10.1002/hep.2437
- Samir, A. E., Dhyani, M., Vij, A., Bhan, A. K., Halpern, E. F., Méndez-Navarro, J., Corey, K. E., & Chung, R. T. (2015). Shear-wave elastography for the estimation of liver fibrosis in chronic liver disease: determining accuracy and ideal site for measurement. *Radiology*, 274(3), 888–896. https://doi.org/10.1148/radiol.14140839.
- Toyoda, H., Kumada, T., Kamiyama, N., Shiraki, K., Takase, K., Yamaguchi, T., & Hachiya, H. (2009). B-mode ultrasound with algorithm based on statistical analysis of signals: evaluation of liver fibrosis in patients with chronic hepatitis C. AJR. American journal of roentgenology, 193(4), 1037–1043. https://doi.org/10.2214/AJR.07.4047
- Tuguntaev, R. G., Hussain, A., Fu, C., Chen, H., Tao, Y., Huang, Y., Liu, L., Liang, X. J., & Guo, W. (2022). Bioimaging guided pharmaceutical evaluations of nanomedicines for clinical translations. *Journal of nanobiotechnology*, 20(1), 236. https://doi.org/10.1186/s12951-022-01451-4
- Ullah, A., Chen, G., Yibang, Z., Hussain, A., Shafiq, M., Raza, F., Liu, D., Wang, K., Cao, J., & Qi, X. (2022). A new approach based on CXCR4-targeted combination liposomes for the treatment of liver fibrosis. *Biomaterials science*, 10(10), 2650–2664. https://doi.org/10.1039/d2bm00242f
- Vernon, G., Baranova, A., & Younossi, Z. M. (2011). Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Alimentary pharmacology & therapeutics*, 34(3), 274–285. https://doi.org/10.1111/j.1365-2036.2011.04724.x
- Younossi, Z. M., Koenig, A. B., Abdelatif, D., Fazel, Y., Henry, L., & Wymer, M. (2016). Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology (Baltimore, Md.)*, 64(1), 73–84. https://doi.org/10.1002/hep.28431
- Younossi, Z., Anstee, Q. M., Marietti, M., Hardy, T., Henry, L., Eslam, M., George, J., & Bugianesi, E. (2018). Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. *Nature reviews*. *Gastroenterology & hepatology*, 15(1), 11–20. https://doi.org/10.1038/nrgastro.2017.109
- Yasaka, K., Akai, H., Kunimatsu, A., Abe, O., & Kiryu, S. (2018). Deep learning for staging liver fibrosis on CT: a pilot study. *European radiology*, 28(11), 4578–4585. https://doi.org/10.1007/s00330-018-5499-7
- Yanguas, S. C., Cogliati, B., Willebrords, J., Maes, M., Colle, I., van den Bossche, B., de Oliveira, C. P. M. S., Andraus, W., Alves, V. A. F., Leclercq, I., & Vinken, M. (2016). Experimental models of liver fibrosis. Archives of toxicology, 90(5), 1025–1048. https://doi.org/10.1007/s00204-015-1543-4
- Zheng, Y., Wu, J., Ding, C., Xu, K., Yang, S., & Li, L. (2020). Disease burden of chronic hepatitis B and complications in China from 2006 to 2050: an individual-based modeling study. *Virology journal*, 17(1), 132. https://doi.org/10.1186/s12985-020-01393-z