Research Article

iMedPub Journals
www.imedpub.com

Health Science Journal
ISSN 1791-809X

2021
Vol. 15 No. 3: 817

# Factors Influencing Transient Elastography in Detecting Liver Stiffness

**Anoop KV*, Krishnadas Devadas and Jijo Varghese**

DM Gastroenterology, Government Medical College Thiruvananthapuram, India

***Corresponding author:**
Anoop KV

anoop85kv@yahoo.com

**Tel:** +918129459041

Medical Gastroenterology, Medical College Trivandrum 695011, India

**Citation:** Anoop KV, Devadas K, Varghese J (2021) Factors Influencing Transient Elastography in Detecting Liver Stiffness. Health Sci J. 15 No. 3: 817.

## Abstract

Transient elastography (TEE) is a method used for estimating liver fibrosis by measuring the liver stiffness (LSM). Aim of this study was to investigate whether TEE fibrosis scores and liver biopsy fibrosis scores are comparable. It was a Cross sectional study of patients undergoing liver biopsy because of high TEE with persistent transaminitis/normal TEE with persistent transaminitis/high TEE with normal transaminases. TEE fibrosis score of study population was compared to liver biopsy fibrosis scores, which is considered as gold standard, and patients with discordance of more than one fibrosis stage was analyzed with above mentioned variables which can affect TEE. Characteristics of the discordant population was analysed. After applying spearman´s correlation it was found that albumin, Total bilirubin and INR had a strong correlation with TEE values. Multiple regression analysis showed albumin and SGOT were independent predictors of Liver stiffness measurement. The discordant population was again analysed after classifying it into two groups i.e F 0-2 (minimal fibrosis) and F 3 (significant fibrosis based on biopsy). After analysis it was found that in F 0-2 group there were certain variables like SGPT, Albumin and INR which had strong correlation with TEE values. Total bilirubin and platelets had moderate correlation with TEE values. After analysing F3 group, age had strong positive correlation with TEE values. TEE was found to be better in detecting liver stiffness than liver biopsy in clinically suspected cirrhosis in this study.

**Keywords:** Fibro scan; Liver stiffness; Fibrosis

**Received with Revision** March 01, 2021, **Accepted:** March 15, 2021, **Published:** March 19, 2021

## Introduction

Liver inflammation is commonly associated with fibrosis [1-3]. The clinical manifestations of liver fibrosis and cirrhosis are different. Minimal liver fibrosis can be completely asymptomatic, but severe fibrosis can present t as hepatic failure. Likewise, earlycirrhosis may not have any specific symptoms and signs; but advancedcirrhosis has multiple presentations of hepatic decompensation, in the form ofhepatic encephalopathy, variceal hemorrhage, spontaneous bacterial peritonitis, and hepatocellular carcinoma [4,5].

Based on data from G D'Amico et al, we have substages within compensated cirrhosis (stage 1 and 2) and decompensated cirrhosis (stages 3 and 4). Stage 1 iscompensated cirrhosiswithout varices, whereas Stage 2 is compensated cirrhosis with varices, but without variceal haemorrhage). Both the substages have a low one-year mortality of 1% and 3% respectively. Stage 3 consists of cirrhosis patients with ascites (with or without varices) but without variceal haemorrhage and stage 4 comprises of cirrhosis patients presenting with variceal haemorrhage (with or without ascites) [6]. They have a higher one-year mortality of 20% and 57% respectively. This classification implies on the fact that, timely diagnosis of cirrhosis is very important as it has significant impact on prognosis and treatment of the patient.

A multicenter study was conducted for evaluating the etiology of chronic liver diseases in India. Eleven hospitals were involved in the study. Alcoholism was the commonest cause of cirrhosis in india. Hepatitis B was the commonest cause of chronic liver disease in general. The predominant causes of chronic liver disease in india were different in different areas. Hepatitis C was common in North india while hepatitis B was the commonest causein East and South india. Alcohol was common in North-east and Non-alcoholic Fatty Liver Disease was the commonest etiology of CLD in Western part of the country.

Since liver fibrosis has significant impact in prognostication of chronic liver disease, assessing liver fibrosis by fibro scan is imperative in creating a treatment plan for the patient. Even though liver biopsy is considered as the available gold standard in assessing liver fibrosis, certain issues like complications associated with liver biopsy (bleeding, pneumothorax, and procedure-related death) [7,8], inter- and intra-observer variability [9], sampling

 

errors has limited its use. Therefore the need for a non invasive method to assess liver fibrosis has been increased. Transient elastography (TEE) is a safe and prompt method to evaluate liver fibrosis by measuring the liver stiffness [10]. Fibro scan has previously been used to evaluate the degree of liver fibrosis in patients with different etiologies like hepatitis B [11], hepatitis C [12,13] alcoholic liver disease [14,15] and autoimmune liver diseases [16]. Fibro scan has also been used for assessing decrease in liver stiffness after a successful antiviral therapy in hepatitis C [17,18]. There are certain factors which can affect the Liver Stiffness Measurement (LSM). There have been multiple studies in the past to identify the factors which can affect the Liver Stiffness Measurement (LSM). So interpreting a TEE value should be based on these clinical and biochemical parameters also in order to correctly identify liver Stiffness.

Although liver biopsy is considered as the gold standard for detecting liver fibrosis, its not widely used in clinical practice since it is an invasive modality. Marcellin et al [19-21] found out that fibroscan is an effective method for detecting fibrosisin Hepatitis Bpatients. In a study by Rongshan et al [22] the factors influencing Fibro scan detection were studied. The results revealed that platelet levels, albumin, INR and body mass index were independent predictors of liver stiffness. This shows that, there are certain parameters which can affect the accuracy of transient elastography in detecting liver stiffness.

A meta-analysis by Tsochatzis et al [23] showed that transient elastography results should be used with caution since there is no validation of the stiffness cut-offs for the various stages of liver fibrosis and cirrhosis. In a study by Sagir et al. [24], it was found that that the Liver stiffness increased in patients with acute liver injury, suggesting that Fibroscan results are not suitable for detecting cirrhosis/fibrosis in these patients. Myer et al conducted a study for assessing the discordance in fibrosis staging by transient elastography and liver biopsy. They found out that mild fibrosis, and higher body mass index (BMI), SGPT and LSM variability [assessed by the ratio of the interquartile range to median LSM (IQR/M)] were independently associated with discordance [25]. Gaia s et al study concluded that fibro scan can be considered as an alternative to liver biopsy in detecting fibrosis in Chronic hepatitis C patients, but host or disease-related factors may modify accuracy of TEE results in Chronic hepatitis B and Non alcoholic fatty liver disease (NAFLD) patients [26]. Bae RC et al. study revealed that age, GGT, and albumin are the clinical factors which influence LSM values [27]. Even though Liver biopsy is considered as the available gold standard in assessing liver fibrosis, certain issues like complications associated with liver biopsy (bleeding, pneumothorax, and procedure-related death), inter- and intra-observer variability, sampling errors has limited its use. TEE has the advantages of being painless, rapid, and easy to perform at the bedside or in the outpatient clinic [28-53].

There are a lot of other factors which can influence TEE scores which include hepatitis, cholestasis, cardiac failure, nonfasting status, Operator effect etc. Acute hepatitis may lead to an increase in liver stiffness without significant fibrosis on liver biopsy [54]. Study conducted by G. Millonig et al and A. Trifan et al [55,56] showed that liver stiffness decreased after successful cholestasis drainage and thereby demonstrated that stiffness is related to bilirubin levels also. Inter-observer agreement was significantly reduced in patients with lower degrees of liver fibrosis (intra-class correlation coefficients (ICC) for F0–1 and F2 were 0.60 and 0.99, respectively)[57].

# Materials and Methods

## Clinical data of subjects

This was a cross sectional study conducted in Government medical college, Trivandrum from the time period of 1/04/2017 to 31/03/2018.Among the 92 patients studied,51 patients were males and 41 were females. Among the study population, we had 45 (49 %)patients with Non Alcoholic Steatohepatitis, 24 (26 %) patients with Chronic Hepatitis B, 12(13 %) patients with Chronic Hepatitis C and 11 (12 %) patients with Autoimmune Hepatitis as the etiology of liver disease. The average age of the population was 42.1. The present study was conducted in accordance with the Declaration of Helsinki, and with approval from the Ethics Committee of Government medical college, Trivandrum. Written informed consent was obtained from all participants (**Table 1**).

Patients with Chronic liver disease of any etiology except Hepatitis B who underwent liver biopsy because of (1)persistent transaminitis (>6 months) and high Transient elastography fibrosis score, (2) normal transaminases and high Transient elastography fibrosis score, (3) persistent transaminitis and normal Transient elastography fibrosis score, (4) For diagnosis (Autoimmune hepatitis, NASH), (5) Hepatitis B patients included in the study were those who underwent liver biopsy because of normal ALT and TEE score between 6-9KPa and high ALT but <5 times upper limit normal with TEE score between 6-12KPa [28]. Patients not willing to give consent for liver biopsy and patients with severe coagulopathy were excluded from the study.

## Clinical information and biochemical examination

Patients with chronic liver disease who underwent liver biopsy was selected for the study and the following study variables was collected like Gender, Age, BMI, Skin fold thickness over right lower lateral rib cage, Waist circumference, CBC, RFT, LFT/INR,

**Table 1** Table showing Characteristics of the study population.

| Characteristics of the study population | Mean values |
|---|---|
| Age | 42.1 |
| BMI | 23.5 kg/m2 |
| TEE score | 16.3 kpa |
| Hemoglobin | 12.9 g/dl |
| Platelets | 1.85 lakhs |
| Total bilirubin | 1.65 mg/dl |
| Direct bilirubin | 0.95 mg/dl |
| SGOT | 78 IU/L |
| SGPT | 110 IU/L |
| Alkaline phosphatase | 117 IU/L |
| Total protein | 7.05 g/dl |
| Albumin | 3.5 g/dl |
| INR | 1.145 |

Etiology of chronic liver disease, Fibroscan- Transient elastography fibrosis score (within 3 months of liver biopsy) [29], Liver biopsy fibrosis score (Metavir score).

### How fibro scan measurement was done?

Liver stiffness measurement was done with M probe after atleast 4 hrs of fasting. Transient elastography was performed on the right lobe of the liver with patient in dorsal decubitus position and measurement done in intercostal spaces. The operator locates the probe in a liver portion at least 6 cm thick and free of large vascular structures and gallbladders. 10 valid measurements were taken and the median value of the ten valid measurements (VM) was considered representative of liver stiffness. The success rate was calculated as the number of valid measurements divided by the total number of measurements. Success rate more than 60% was considered reliable. The results were expressed in kilopascals (kPa) [30].

Interquartile range (IQR) was defined as an index of intrinsic variability of LSM corresponding to the interval of LSM results containing 50% of the valid measurements between the 25th and 75th percentiles. Only LSMs with at least 10 VMs were considered reliable. Any LSM that did not meet these criteria of reliability were excluded [31]. In the present study, a single experienced operator, who was blinded to patients' clinical data and Liver biopsy results, performed all Liver stiffness measurements. An operator with minimal operator training (≥10 observed scans on patients) was used in the study [37].

### Statistical analysis

All the data were analysed by SPSS version 23.0 software (SPSS, inc, chicago, IL, USA).The correlation between Liver stiffness measurement and variables was analys by spearman´s correlation. Multiple regression analysis also was used to analyse the predictors affecting transient elastography detection and to obtain the multiple regression equation. Differences with P <0.05 was considered as statistically significant.

## Results

Baseline demographics and characteristics: Among the 92 patients studied, 51 patients were males and 41 were females. Among the study population, Ihad 45 (49 %)patients with Non Alcoholic Steatohepatitis, 24 (26 %) patients with Chronic Hepatitis B, 12 (13%) patients with Chronic Hepatitis C and 11 (12%) patients with Autoimmune Hepatitis as the etiology of liver disease. The average age of the population was 42.1.

The population had average Transient Elastography scoreof 16.3 kpa, BMI 23.5 kg/m2, Hemoglobin 12.9 g/dl, platelet count 1.85 lakhs, Total bilirubin 1.65 mg/dl, Direct bilirubin 0.95 mg/dl, SGOT 78 IU/L, SGPT 110 IU/L, Alkaline Phosphatase 117 IU/L, Total Protein 7.05 g/dl, Albumin 3.5 g/dl and INR 1.145. Among the study population 44 patients had a discordance of one or more fibrosis stage with Transient elastography from the liver biopsy score, which was taken as the gold standard for deciding the liver fibrosis/cirrhosis. Among them there were 24 NASH, 9 CHB, 5 CHC and 6 AIH patients.

## Analysis

Among the study population, 44 (47.8%) patients had discordant TEE scores and biopsy scores. The characteristics of the population with discordant values were analysed. After applying Spearmans correlation, certain variables had positive or negative correlation with Transient Elastography scores. Among the variables analysed albumin had a Spearman's correlation coefficient of -0.778 (strong negative correlation) (p value - 0.000), Total bilirubin which had a Spearman's correlation coefficient of 0.602 (strong positive correlation) (p value- 0.002), INR which had a Spearman's correlation coefficient of 0.754 (strong positive correlation) (p value-0.03).

Platelets had a Spearman's correlation coefficient of -0.436 (moderate negative correlation), SGOT had a value of 0.565 (moderate positive correlation), Total protein had a value of -0.479 (moderate negative correlation), waist circumference had a value of 0.453 (moderate positive correlation). Age had a Spearman's correlation coefficient of 0.317(weak positive correlation), SGPT had a value of0.393 (weak positive correlation), BMI had a value of 0.398 (weak positive correlation).Multiple regression analysis was then performed on the indexes of age, BMI, Hemoglobin, Platelets, SGOT, SGPT, GGT, Alkaline phosphatase, Total protein, Albumin, Total bilirubin, waist circumference and INR. **Table 2** demonstrates that the effects of Albumin and SGOT on Liver stiffness measurement (LSM) were statistically significant (all P value < 0.05).Thus it was found that albumin and SGOT were independent predictors of Liver stiffness measurement (LSM).

The discordant population was again analysed after classifying it into two groups i.e F 0-2 (minimal fibrosis) and F 3 (significant fibrosis based on biopsy) (There was no patient in F4 group). After analysis it was found that in F 0-2 group there was certain variables like SGPT (0.608 -positive correlation), Albumin (-0.659 – negative correlation), INR (0.66 – positive correlation) which had strong correlation with TEE values. Total bilirubin (0.455) and platelets (- 0.518) had moderate correlation with TEE values. Age (0.248), SGOT (0.355), Total protein (-0.392) and BMI (0.225) had weak correlation with TEE values.

After analysing F3 group, age (0.775) had strong positive correlation, total protein (-0.434) had moderate negative correlation, platelets (-0.25 –weak negative correlation) and INR (0.355- weak positive correlation) with TEE values. Transient elastography was better than liver biopsy in detecting liver stiffness in clinically suspected cirrhosis in this study.

**Table 2** Multiple regression analysis results of liver stiffness measurement influencing factors.

| Characteristics of the study population | P value |
|---|---|
| BMI | 0.92 |
| Platelets | 0.335 |
| Total bilirubin | 0.162 |
| SGOT | 0.009 |
| SGPT | 0.080 |
| Albumin | 0.002 |
| INR | 0.446 |
| Waist circumference | 0.829 |

## Discussion

Fibro scan is a non-invasive method for assessing liver stiffness, which is used as an alternative method to liver biopsy. Not only liver fibrosis but also other factors contribute to liver stiffness. In the present study certain factors which can influence the accuracy of Transient elastography were analysed. After applying Spearman´s correlation I found that certain factors like Age, BMI, Albumin, SGOT, SGPT, INR, platelets, Total bilirubin, Waist circumference had correlation with Transient elastography scores and can influence TEE values. Through multiple regression analysis, the two factors Albumin and SGOT were found to be independent predictors of Liver Stiffness Measurement (LSM).

Platelets production is affected by thrombopoietin which is synthesized by hepatocytes. With the development of liver tissue fibrosis, thrombopoietin levels decrease and cause thrombocytopenia [40,41]. Liver is the organ were albumin is synthesised and bilirubin is excreted. Both are affected as fibrosis progresses. Hencealbumin had a negative correlation and bilirubin has a positive correlation with Transient elastography scores.

All blood coagulation factors with the exception of calcium ions and factor VIIa, are synthesized in the liver. INR is another factor which can be affected once the patient develops cirrhosis and it was found in the study to have a positive correlation with Transient elastography scores. Fatty liver can progress into liver fibrosis and cirrhosis [42]. In obese individuals, the thickness of fat layer on the abdominal wall may lead to overestimation of the LSM value. But in my study it was found that Skin fold thickness (over the site where Fibro scan probe is kept) was found to have no significant correlation with Transient elastography scores. BMI and waist circumference had a positive correlation with Transient elastography scores in the study.

Hepatitis which is characterised by a 10 fold rise in SGOT and SGPT, can falsely increase the LSM [39]. Igot a positive correlation of TEE scores with SGOT and SGPT values. LSM has been found to be falsely elevated in acute hepatitis, manifested as SGOT and SGPT flares [43,44]. Severe hepatitis can lead to LSM values well within the cirrhotic range, even in the absence of fibrosis on histology [45,46]. Therefore reading a LSM value in this setting should be careful and the clinician has to wait till transa minitis subsides or falls below five times upper limit normal [47,48].

Multiple regression analysis which was performed on the indexes of age, BMI, Hemoglobin, Platelets, SGOT, SGPT, GGT, Alkaline phosphatase, Total protein, Albumin, Total bilirubin, waist circumference and INR, demonstrated that the effects of Albumin and SGOT on Liver stiffness measurement (LSM) were statistically significant (all P value <0.05).Thus it was found that albumin and SGOT were independent predictors of Liver stiffness measurement (LSM).

However, there were certain limitations in my study. Liver stiffness measurement was done with M probe. In this study 28 patients (30%) had obesity. It has been noted that unreliable LSMs occurs at about 3% and 11.6–18.4% in all TEE examinations and they are independently associated with BMI >30 kg/m$^2$ in both Caucasians and Chinese [49,50]. The success rate of LSMs with the M probe may be less than 75% in NAFLD patients with BMI >30 kg/m$^2$ [51-58]. XL probe was not used in obese population due to unavailability of the probe.

Another limitation of the study was the effect of transaminitis in the range of more than five times upper limit of normal value on TEE values. LSM can be falsely elevated in acute hepatitis, manifested as SGOT and SGPT flares. Severe hepatic necro inflammation may lead to LSM values well within the cirrhotic range, even in the absence of fibrosis on histology. In this study 5 patients had transaminitis in the range of more than five times upper limit of normal value which could have affected the study result.

Transient Elastography was found to be better in detecting liver stiffness than liver biopsy in clinically suspected cirrhosis in this study. This could be because in liver biopsy, the liver tissue samples obtained for biopsy comprise only ~1/50,000 of the entire liver tissue, and therefore may not reflect the condition of the entire liver. The detection capacity of Fibro scan is ~100-fold greater compared with that of liver biopsy, despite the fact that its accuracy is influenced by certain factors.

## Conclusions

In conclusion, Fibro scan is a non-invasive method for assessing liver stiffness, which can be used as an alternative method to liver biopsy. There are certain factors other than liver fibrosis which affects TEE values. Evaluating the degree of liver fibrosis simply based on the LSM value may not be accurate. In patients with minimal fibrosis (F0-2) there were certain confounding factors like SGPT, Albumin and INR which can influence TEE Values. And total bilirubin and platelets had a moderate influence on TEE values. But in patients with significant fibrosis (F3) group there was only one confounding factor like age which could influence TEE values. Transient Elastography was found to be better in detecting liver stiffness than liver biopsy in clinically suspected cirrhosis in this study. The diagnosis and evaluation of liver fibrosis should comprehensively consider the results of Fibro scan along with the clinical and laboratory examination results.

## Conflicts of Interest

None.

## Disclosure of Funding Received for the Work

None.

## References

1 Chen J, Eslick GD, Weltman M (2014) Systematic review with meta-analysis: Clinical manifestations and management of autoimmune hepatitis in the elderly. Aliment Pharmacol Ther 39: 117-124.

2 Aleman S, Rahbin N, Weiland O, Davidsdottir L, Hedenstierna M, et al. (2013) A risk for hepatocellular carcinoma persists long-term after sustained virologic response in patients with hepatitis C-associated liver cirrhosis. Clin Infect Dis 57:230-236.

3 Angeli P, Sanyal A, Moller S, Alessandria C, Gadano A, et al. (2013) International Club of Ascites: Current limits and future challenges in the management of renal dysfunction in patients with cirrhosis: Report from the International Club of Ascites. Liver Int 33:16-23.

4 Wright TL, Lau JY (1993) Clinical aspects of hepatitis B virus infection. Lancet 342:1340-1344.

5 Sharara AI, Hunt CM, Hamilton JD (1996) Hepatitis C. Ann Intern Med 125:658-668.

6 D'Amico G, Garcia-Tsao G, Pagliaro L (2006) Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol 44:217-231.

7 McGill DB, Rakela J, Zinsmeister AR, Ott BJ (1990) A 21-year experience with major hemorrhage after percutaneous liver biopsy. Gastroenterology 99:1396-1400.

8 Jin SY (2007) Role of liver biopsy in the assessment of hepatic fibrosis--its utility and limitations. Korean J Hepatol 13:138-145.

9 Regev A, Berho M, Jeffers LJ, Milikowski C, Molina EG, et al. (2002) Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. Am J Gastroenterol 97:2614-2618.

10 Castéra L, Vergniol J, Foucher J, Le Bail B, Chanteloup E, et al. (2005) Prospective comparison of transient elastography, Fibrotest, APRI, and liver biopsy for the assessment of fibrosis in chronic hepatitis C. Gastroenterology 128:343-350.

11 Degos F, Perez P, Roche B, Mahmoudi A, Asselineau J, et al. (2010) Diagnostic accuracy of FibroScan and comparison to liver fibrosis biomarkers in chronic viral hepatitis: A multicenter prospective study (the FIBROSTIC study). J Hepatol 53:1013-1021.

12 Sebastiani G, Halfon P, Castera L, Pol S, Thomas DL, et al. (2009) SAFE biopsy: A validated method for large-scale staging of liver fibrosis in chronic hepatitis C. Hepatology 49:1821–1827.

13 Bonder A, Afdhal NH (2013) Biopsy no more; changing the screening and diagnostic algorithm for hepatitis C. Clin Gastroenterol Hepatol 11:309-310.

14 Nguyen-Khac E, Chatelain D, Tramier B, Decrombecque C, Robert B, et al. (2008) Assessment of asymptomatic liver fibrosis in alcoholic patients using Fibroscan: Prospective comparison with seven non-invasive laboratory tests. Aliment PharmacolTher2 8:1188-1198.

15 Mueller S, Millonig G, Sarovska L, Friedrich S, Reimann FM, et al. (2010) Increased liver stiffness in alcoholic liver disease: Differentiating fibrosis from steatohepatitis. World J Gastroenterol 16:966-972.

16 Obara N, Ueno Y, Fukushima K, Nakagome Y, Kakazu E, et al. Transient elastography for measurement of liver stiffness measurement can detect early significant hepatic fibrosis in Japanese patients with viral and nonviral liver diseases. J Gastroenterol 43:720-728.

17 Vergniol J, Foucher J, Mamou K, Castéra L, Bernard PH, et al. (2008) Non-invasive evaluation of liver fibrosis using FibroScan in long-term sustained-virological responder patients after HCV treatment. Gastroenterol Clin Biol 32:1061-1063.

18 Wang JH, Changchien CS, Hung CH, Tung WC, Kee KM, et al. (2010) Liver stiffness decrease after effective antiviral therapy in patients with chronic hepatitis C: Longitudinal study using Fibro Scan. J Gastroenterol Hepatol 25:964–969.

19 Yeh WC, Li PC, Jeng YM, Hsu HC, Kuo PL, et al. (2002) Elastic modulus measurements of human liver and correlation with pathology. Ultrasound Med Biol 28:467-474.

20 Jung KS, Kim SU (2012) Clinical applications of transient elastography. ClinMolHepatol18: 163–173.

21 Marcellin P, Ziol M, Bedossa P, Douvin C, Poupon R, et al. (2009) Non-invasive assessment of liver fibrosis by stiffiness measurement in patients with chronic hepatitis B. Liver Int 29:242-247.

22 Shan R, Yin H, Yang W,Li J,Zhang M, et al. (2016) Influencing factors of transient elastography in detecting liver stiffness, ExpTher Med 12: 2302-2306.

23 Tsochatzis EA, Gurosamy KS, Ntaoula S, Cholongitas E, Davidson BR, et al. (2011) Elastography for the diagnosis of severity of fibrosis in chronic liver disease: A meta-analysis of diagnostic accuracy. J Hepatol 54:650-659.

24 Sagir A, Erhardt A, Schmitt M, Häussinger D (2008) Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage. Hepatology 47:592-595.

25 Myers RP, Crotty P, Pomier-Layrargues G, Ma M, Urbanski SJ, et al. (2010) Prevalence, risk factors and causes of discordance in fibrosis staging by transient elastography and liver biopsy. Liver Int 30:1471-1480.

26 Gaia S, Carenzi S, Barilli AL, Bugianesi E, Smedile A, et al. (2011) Reliability of transient elastography for the detection of fibrosis in non-alcoholic fatty liver disease and chronic viral hepatitis. J Hepatol 54:64-71.

27 Bae RC, Cho HJ, Oh JT, Lee EK, Heo J, et al. (2010) Clinical factors influencing liver stiffness as measured by transient elastography (Fibroscan) in patients with chronic liver disease. Korean J Hepatol 16:123-130.

28 EASL-ALEH. Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. J Hepatol 63:237-264.

29 Pavlov CS, Casazza G, Nikolova D, Tsochatzis E, Burroughs AK, et al. (2015) Transient elastography for diagnosis of stages of hepatic fibrosis and cirrhosis in people with alcoholic liver disease. Cochrane Database Syst Rev 2015: CD010542.

30 Reddy JK, Rao MS (2006) Lipid metabolism and liver inflammation. II. Fatty liver disease and fatty acid oxidation". Am J Physiol Gastrointest Liver Physiol 290: G852-858.

31 Hamer OW, Aguirre DA, Casola G, Lavine JE, Woenckhaus M, et al. (2006) Fatty liver: imaging patterns and pitfalls. Radio Graphics 26.

32 Bianchi L (1980) Chronic hepatitis. Schweiz Med Wochenschr 110:1361-1365.

33 Wiegand J, Berg T (2013) The etiology, diagnosis and prevention of

liver cirrhosis: part 1 of a series on liver cirrhosis. Dtsch ArztebllInt 110: 85-91.

34 Centers for disease control and prevention.

35 (2012) STEP wise approach to surveillance (STEPS). World Health Organization.

36 Alberti K, Zimmet P, Shaw J (2005) IDF Epidemiology Task Force Consensus Group. The metabolic syndrome - a new worldwide definition. Lancet 366: 1059-1062.

37 Armstrong MJ, Corbett C, Hodson J, Marwah N, Parker R, et al. (2013) Operator training requirements and diagnostic accuracy of Fibroscan in routine clinical practice. Postgrad Med J 89:685-692.

38 Bedossa P, Poynard T (1996) An algorithm for grading activity in chronic hepatitis C.The METAVIR Cooperative Study Group. Hepatology 24:289-229.

39 Wong GL (2013) Update of liver fibrosis and steatosis with transient elastography (Fibroscan). Gastroenterol Rep (Oxf) 1:19-26.

40 Tana MM, Zhao X, Bradshaw A, Moon MS, Page S, et al. (2015) Factors associated with the platelet count in patients with chronic hepatitis C. Thromb Res 135:823-828.

41 Lu SN, Wang JH, Liu SL, Hung CH, Chen CH, et al. (2006) Thrombocytopenia as a surrogate for cirrhosis and a marker for the identification of patients at high-risk for hepatocellular carcinoma. Cancer 107:2212-2222.

42 Henderson NC, Iredalc JP (2007) Liver fibrosis: Cellular machanisms of progression and resolution. Clin Sci (Lond) 112:265-280.

43 Coco B, Oliveri F, Maina AM, Ciccorossi P, Sacco R, et al. (2007) Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. J Viral Hepat 14:360-369.

44 Wong GL, Wong VW, Choi PC, Chan AWH, Chum RHL, et al. (2008) Assessment of fibrosis by transient elastography compared with liver biopsy and morphometry in chronic liver diseases. Clin Gastroenterol Hepatol 6:1027-1035.

45 Arena U, Vizzutti F, Corti G, Ambu S, Stasi C, et al. (2008) Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology 47:380-384.

46 Sagir A, Erhardt A, Schmitt M, Häussinger D (2008) Transient elastography is unreliable for detection of cirrhosis in patients with acute liver damage. Hepatology 47:592-595.

47 Chan HL, Wong GL, Choi PC, Chan AW, Chim AM, et al. (2009) Alanine aminotransferase-based algorithms of liver stiffness measurement by transient elastography (Fibroscan) for liver fibrosis in chronic hepatitis B. J Viral Hepat 16:36-44.

48 Wong GL, Wong VW, Choi PC, et al. (2008) Assessment of fibrosis by transient elastography compared with liver biopsy and morphometry in chronic liver diseases. Clin Gastroenterol Hepatol 6:1027-1035.

49 Castera L, Foucher J, Bernard PH, Carvalho F, Allaix D, et al. (2010) Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. Hepatology 51:828-835.

50 Wong GL, Wong VW, Chim AM, You KK, Chu ST, et al. (2011) Factors associated with unreliable liver stiffness measurement and its failure with transient elastography in the Chinese population. J Gastroenterol Hepatol 26:300-305.

51 Wong VW, Vergniol J, Wong GL, Foucher J, Chan HL, et al. (2010) Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. Hepatology 51:454-462.

52 Fraquelli M, Rigamonti C, Casazza G, Conte D, Donato MF, et al. (2007) Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut 56:968-973.

53 Sandrin L, Fourquet B, Hasquenoph JM, Yon S, Fournier C, et al. (2003) Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. Ultrasound Med Biol 29:1705-1713.

54 Arena U, Vizzutti F, CortiG, Ambu S, Stasi C, et al. (2008) Acute viral hepatitis increases liver stiffness values measured by transient elastography. Hepatology 47: 380-384.

55 Millonig G, Reimann FM, Friedrich S, Fonouni H, Mehrabi A, et al. (2008) Extrahepatic cholestasis increases liver stiffness (fibroScan) irrespective of fibrosis. Hepatology 48: 1718-1723.

56 Trifan A, Sfarti C, Cojocariu C, Dimache M, Cretu M, et al. (2011) Increased liver stiffness in extrahepatic cholestasis caused by choledocholithiasis. Hepat Mon11: 372-375.

57 Fraquelli M, Rigamonti C, Casazza G, Conte D, Donato MF, et al. (2007) Reproducibility of transient elastography in the evaluation of liver fibrosis in patients with chronic liver disease. Gut 56:968-973.

58 Mukherjee PS, Vishnubhatla S, Amarapurkar DN, Das K, Sood A, et al. (2017) Etiology and mode of presentation of chronic liver diseases in India: A multi centric study.Partha S. Mukherje, PLoS One 12:e0187033.