Sohag University | Sohag Medical Journal | Faculty of Medicine

Review Article

# Use of Transient Elastography in Assessment of Non Alcoholic Fatty Liver Disease

**Noha M. Abd EL Rahman[1], Ghada M Galal[2], Ramy Mamdouh El Sharkawy[1] and Sherif Abd El Aziz Sayed[3]**

1-Department of Tropical Medicine and Gastroenterology, Faculty of Medicine, Sohag University
2- Department of Tropical Medicine and Gastroenterology, Faculty of Medicine, Assiut University
3-Department of Clinical Pathology, Faculty of Medicine, Sohag University

## Abstract:

The most prevalent chronic liver disease globally is non-alcoholic fatty liver disease (NAFLD). It is frequently regarded as the hepatic component of metabolic syndrome and is connected to obesity, $T_2$DM and dyslipidemia. Among NAFLD patients there are 2 categories simple steatosis and non-alcoholic steatohepatitis (NASH), the later can lead to cirrhosis. The gold standard for identifying NASH and distinguishing it from simple steatosis is a liver biopsy, but it is intrusive and costy. New methods for evaluating NAFLD, the presence or absence of NASH and the severity of any comorbid fibrosis or cirrhosis must be developed. In this review, we'll demonstrate how to use transient elastography technique in FibroScan as a non-invasive tool (method) to identify patients with early disease from those progressed to fibrosis.

**Aim of the work:**

To clarify the clinical application of FibroScan as a non-invasive imaging tool for the evaluation and diagnosis of NAFLD and to highlight any potential drawbacks.

**Keywords:** NAFLD, NASH, TE

**DOI : 10.21608/SMJ.2023.238958.1418**

*Correspondence : ali80759@gmail.com

Received: 08 Octobe 2023
Revised: 16 October 2023
Accepted: 16 October 2023
Published: 01 January 2023

## Introduction:

NAFLD is estimated to affect about 25% of the global population, making it the most prevalent chronic liver disease. (1)

In the absence of any other causes of liver illness, NAFLD is characterized by the presence of hepatic steatosis affecting at least 5% of liver cells. The disease range from simple steatosis (NAFL) to the more severe non-alcoholic steatohepatitis (NASH), which affects 10 to 25% of cases. NASH can proceed to liver cirrhosis and other liver-related problems such hepatocellular carcinoma (HCC). (2)

NAFLD can be diagnosed by the following criteria: imaging or histology that detect hepatic steatosis (HS) (with no other etiologies for HS), no concurrent other causes of chronic liver disease, and finally no history of major alcohol consumption. (3)

In order to distinguish simple steatosis from steatohepatitis, which are the first steps on the path to more severe and advanced stages of the disease such as fibrosis and cirrhosis, it is crucial to diagnose the disease as early as possible . (4)

The ideal tool for diagnosing NASH is liver biopsy. Grading and staging are traditionally included in the histological evaluation of NAFLD. Stages include grading of steatosis (from 1-3), fibrosis (from 0-4) and grading of inflammatory activity (from 1-3). [5] Although rare but possible problems and sampling errors are linked to liver biopsy, as it is invasive and expensive . [6]

The degree of fibrosis, cirrhosis as well as the presence or absence of NASH are the main aim for which new tests being developed to evaluate NAFLD. The tests should be non-invasive, precise, repeatable, and reasonably priced to fulfill this goal. These noninvasive tests use serum biomarkers or radiographic techniques. [7]

Ultrasonography, magnetic resonance (MRI) and computed tomography (CT)) all are used in the radiological diagnosis of NAFLD. [8] FibroScan manufacturer has created the controlled attenuation parameter (CAP) technique for reliable steatosis measurement. [9] The measurement is based on the observation that a fatty liver causes the amplitude of ultrasound waves to attenuate more quickly. Additionally, liver stiffness and CAP measurements can be taken simultaneously to assess liver fibrosis with high precision and repeatability. [10]

TE is carried out using a FibroScan instrument. It was the first tool made to assess liver elasticity in place of a biopsy. It is solely devoted to study of fibrosis of the liver. It makes use of a 5 MHz ultrasonic transducer that is mounted on the shaft of a piston that serves as a vibrator. Pushing a button causes low frequency (50 Hz) transient vibrations to be sent, and the resulting elastic shear waves travel through the tissues below. It is used to evaluate the elasticity of tissue in patients with chronic liver disease, to identify the level of fibrosis . [11]

The TE technique assesses liver fibrosis by observing the speed at which ultrasound waves go through the liver; as fibrosis advances, the liver tissue becomes harder and the waves move more quickly. The degree of stiffness and thus the stage of liver fibrosis can be calculated using the wave propagation velocity. The primary ultrasound elastography techniques used to analyze the liver are TE, pSWE, and 2D-SWE. **[12]** There are various types of ultrasound elastography.

The suggestions listed below can be followed when conducting an examination. [13]

**Guidelines for doing hepatic elastography**

- A strict routine must be followed.
- The patient should avoid eating a 4-hour before the exam.
- To widen the intercostal space, the examination s hould be done while the patient supine or slight ly to the left.
- Measurments are taken using an intercostal method at optimal acoustical window location.
- To prevent reverberation artifact, measurements should be obtained 1.5 to 2.0 cm below liver capsule. The optimum place for shear wave generation is between 4.0 to 4.5 cm from the transducer.
- The liver capsule and the transducer should be pe rpendicular.
- Avoid selecting the region of interest near big blood vessels.
- Based on the patient's body habitus, the right tran sducer should be chosen.
- For transient elastography and point shear wave elastography approaches, ten measurments should be taken from ten separate photos taken in the same spot. The median value should be used.
- When a quality assessment parameter is utilized, three or five measurments may be sufficient for 2-D shear wave elastography. For an accurate dataset.
- The IQR/M for measurements of kPa should be <0.3 and for readings of m/s should be <0.15.

The cylindrical volume used for the TE examination's during measuring liver stiffness about 10x40 mm at a depth of 25-65 mm from the skin's surface is significantly more descriptive of the liver parenchyma . [14]

Results taken improperly or with excessive transducer pressure on the skin are automatically removed; they should be taken in a parenchymal region devoid of arteries and bone. As the ultrasonic wave travels through the medium, its intensity exponentially decreases, which means that the more harder the tissue, the faster the vibrations will travel. As a result, the degree of parenchymal

fibrosis in the liver increases with increasing result (in kPa). [11]

TE can distinguish between mild and severe fibrosis. [15] When the interquartile range/median ratio of the values is less than 0.3, liver stiffness assessment with TE is regarded as trustworthy. **[16]** Elderly participants and patients who are overweight or obese are more likely to have unreliable measures. [17]

By utilizing a system-integrated technique to calculate the CAP, TE can be utilized to assess steatosis. [18]

Additionally, CAP's accuracy was superior to the FLI, HSI and to the Steato Test. However, patients with more advanced fibrosis seem to have reduced CAP accuracy . [19]

The CAP method has been shown to be a useful method for evaluating and following patients with NAFLD despite the fact that there have been few studies evaluating it. This is because it is simple to use, can analyze a portion of the liver 100 times larger than the typical liver biopsy specimen, and offers the benefits of operator independence and immediate results . [20] Although patients with less fibrosis, less steatosis, or a high BMI had lower levels of agreement than those with more of these conditions, studies have shown that FibroScan has strong reproducibility. [21]

**Transient elastography's limitations include:**

**1-obesity**

In addition to making it difficult to measure hepatic stiffness, obesity also makes the liver stiffer even when there is no fibrosis. **[22]** Steatosis appears to also influence the assessment of liver stiffness, especially in non cirrhotic patients . **[23]**

Another probe, the XL-probe, has been created to get around these restrictions and offers more accurate measurements in obese patients. **[24]** When compared to the M-probe, the XL-probe produces vibrations with a lower frequency (1.75 MHz vs. 3.5 MHz) and higher amplitude (3 mm vs. 2 mm, respectively), allowing for deeper measurements (3.5-7.5 cm vs. 2.5-6.5 cm, respectively), and producing reliable results in roughly 57%–63% of patients with inaccurate M-probe readings. The precision of diagnosing fibrosis and the reliability of measurements are both declining with an increase in BMI, even when the XL probe is being utilized .**(25)**

**2-Ascites**

Since the shear wave cannot travel through fluid and fat also attenuates ultrasound and elastic waves, TE cannot be performed on ascites patients and is linked to greater failure rates or incorrect results when performed on obese patients with the usual M probe . [26]

**3- Children**

In order to increase dependability in this area, novel pediatric S2 probes are now readily available. Children and slim patients with limited intercostal gaps also have greater failure rates. [27]

**4-Acute inflammation**

It should be noted that data indicate that liver stiffness values for TE may be 1.3–3 times higher in the presence of acute inflammation and/or moderate alanine aminotransferase (ALT) elevation . **[28]** As a result, the use of TE in the presence of transaminitis is not advised. [29, 30]

**5- Other restrictions**

Aside from aging **[33]**, extra hepatic cholestasis **[32]**, and sinusoidal congestion .**[31]** are the other factors that may impair the ability to accurately assess stiffness.

## Conclusions

Early diagnosis of NAFLD in high risk patients can be done by transient elastography. Grading of steatosis and staging of fibrosis can be easily and safely performed. However, current research indicates that different combinations of these procedures may be useful as a cost-effective alternative to liver biopsy, which has a significant associated morbidity and mortality.

## References:

1- Younossi ZM, Koenig AB, Abdelatif D, et al. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. 2016; 64:73-84.

2- Spengler EK and Loomba R. Recommendations for diagnosis, referral for liver biopsy, and treatment of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Mayo Clin Proc 2015;90:1233-1246.

3- Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. Gastroenterology. 2012; 142:1592-1609.

4- Manousou P, Kalambokis G, Grillo F, et al. Serum ferritin is a discriminant marker for both fibrosis and inflammation in histologically proven non-alcoholic fatty liver disease patients. Liver Internat 2011; 31:730-9.

5- American Gastroenterological Association. AGA technical review on Nonalcoholic Fatty Liver Disease. Gasteroenterology 2002;123: 1705-1725.

6- Pearce SG, Thosani NC and Pan JJ. Noninvasive biomarkers for the diagnosis of steatohepatitis and advanced fibrosis in NAFLD. Biomarker Research 2013; 4;1(1):7.

7- Chan HL and Wong VW. Non invasive methods to determine the severity of NAFLD and NASH. In: Farrel GC, Mc Cullough AJ, Day CP, eds. Non alcoholic fatty liver disease: a practical guide. United Kingdom: Wiley–Blackwell 2013; 112-21.

8- Li Q, Dhyani M, Grajo JR, et al. Current status of imaging in nonalcoholic fatty liver disease. World J Hepatol 2018; 10: 530-542.

9- Kwok R, Tse YK, Wong GL, et al. Systematic review with meta analysis: non invasive assessment of non alcoholic fatty liver disease the role of transient elastography and plasma cytokeratin-18 fragments. Aliment Pharmacol Ther 2014; 39:254-269.

10- Chan TT and Wong VW. In search of new biomarkers for nonalcoholic fatty liver disease. Clinical liver disease 2016; 8:19-23.

11- Piscaglia F, Marinelli S, Bota S, et al. The role of ultrasound elastographic techniques in chronic liver disease: current status and future perspectives. Eur J Radiol 2014;83:450-5.

12- Silva LCM, Oliveira JT, Tochetto S, et al. Ultrasound elastography in patients with fatty liver disease. Radiol Bras 2020;53:47-55.

13- Ferraioli G, Wong ONG, Castera l, et al. Liver Ultrasound Elastography: An update to the world federation for ultrasound in medicine and biology guidelines and recommendations. Ultrasound in Med & Biol 2018;44:2419-2440.

14- Vergniol J, Foucher J, Terrebonne E, et al. Noninvasive tests for fibrosis and liver stiffness predict 5-year outcomes of patients with chronic hepatitis C. Gastroenterology 2011;140:1970-9.

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

16- Boursier J, Zarski JP, de Ledinghen V, et al. Determination of reliability criteria for liver stiffness evaluation by transient elastography. Hepatology. 2013; 57:1182-91.

17- de Lédinghen V, Vergniol J, Foucher J, et al. Non-invasive diagnosis of liver steatosis using controlled attenuation parameter (CAP) and transient elastography Liver Int. 2012; 32:911-918.

18- Karlas T, Petroff D, Garnov N et al. Non-invasive methods for the diagnosis of NAFLD WJH|www.wjgnet.com 647 April 8, 2015, 7, 4.

19- Myers RP, Pollett A, Kirsch R, et al. Controlled Attenuation Parameter (CAP): a noninvasive method for the detection of hepatic steatosis based on transient elastography. Liver Int 2012; 32:902-910.

20- Lupsor-Platon M, Stefanescu H, Muresan D, et al. Noninvasive assessmentof liver steatosis using ultrasound methods. Med Ultrason 2014; 16: 236-45.

21- Franzese A, Vajro P, Argenziano A, et al. Liver involvement inobese children. Ultrasonography and liver enzyme levels at diagnosisand during follow-up in an Italian population. Dig Dis Sci 1997; 42:1428-32.

22- Baba M, Furuya K, Bandou H, et al. Discrimination of individuals in a general population at high-risk for alcoholic and non-alcoholic fatty liver disease based on liver stiffness: a cross section study. BMC Gastroenterol 2011; 11:70.

23- Gaia S, Carenzi S, Barilli AL, et al. Reliability of transient elastography for the detection of fibrosis in

non-alcoholic fatty liver disease and chronic viral hepatitis. J Hepatol 2011;54:64-71.

24- Wong VW, Vergniol J, Wong GL, et al. Liver stiffness measurement using XL probe in patients with nonalcoholic fatty liver disease. Am J Gastroenterol. 2012; 107:1862-1871.

25- Şirli R, Sporea I, Deleanu A, et al. Comparison between the M and XL probes for liver fibrosis assessment by transient elastography. Med Ultraso 2014;16:119-122.

26- Stasi C, Arena U, Vizzutti F, et al. Transient elastography for the assessment of liver fibrosis in patients with chronic viral hepatitis: the missing tool? Dig Liver Dis 2009; 41:863-866.

27- Pradhan F, Ladak F, Tracey J, et al. Feasibility and reliability of the FibroScan S2 (pediatric) probe compared with the M probe for liver stiffness measurement in small adults with chronic liver disease. Ann Hepatol 2013;12:100-107.

28- Tapper EB, Cohen EB, Patel K, et al. Levels of alanine aminotransferase confound use of transient elastography to diagnose fibrosis in patients with chronic hepatitis C virus infection. Clin Gastroenterol Hepatol 2012;10:932-937.

29- Coco B, Oliveri F, Maina AM, et al. Transient elastography: a new surrogate marker of liver fibrosis influenced by major changes of transaminases. J Viral Hepat 2007; 14:360-369.

30- Castera L, Forns X, Alberti A. Non-invasive evaluation of liver fibrosis using transient elastography. J Hepatol. 2008; 48:835-847.

31- Lebray P, Varnous S, Charlotte F et al. Liver stiffness is an unreliable marker of liver fibrosis in patients with cardiac insufficiency. Hepatology 2008; 48:2089.

32- Millonig G, Reimann FM, Friedrich S, et al. Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. Hepatology 2008; 48:1718-1723.

33- Kettaneh A, Marcellin P, Douvin C, et al. Features associated with success rate and performance of FibroScan measurements for the diagnosis of cirrhosis in HCV patients: a prospective study of 935 patients. J Hepatol 2007;46:628-634.