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A REVIEW STUDY ON: SONOELASTOGRAPHY IN NONALCOHOLIC FATTY LIVER DISEASE

Arnabjyoti Deva Sarma *Faculty of Paramedical Science (Radiology), Assam downtown University, Guwahati, Assam*
Moitrayee Devi *Faculty of Science (Microbiology), Assam downtown University, Guwahati, Assam*

Abstract: It is an imaging technology sensitive to tissue stiffness that was first described in the 1990s. Nonalcoholic fatty liver disease (NAFLD) is increasingly common around the world, especially in Western nations. In the United States, it is the most common form of chronic liver disease, affecting about one-quarter of the population. In this study we will discuss a review based study on a non-invasive, cost effective technique, without any radiation hazards, to measure the elastic property of liver tissue using ultrasound imaging modality called as sonoelastography in Indian population for assessment of disease severity and grading of nonalcoholic fatty liver disease

Keywords: Ultrasound, Liver, Biopsy, Fibrosis, elastography, liver parenchyma

INTRODUCTION:

Fatty Liver Disease is emerging as an important cause of liver disease in northern India. Epidemiological studies suggest prevalence of nonalcoholic fatty liver disease (NAFLD) in around 9% to 32% of general population in India with higher prevalence in those with overweight/ obesity and diabetes/ pre-diabetes. [1] NAFLD is a common clinico-pathological condition characterized by significant lipid deposition in the hepatocytes of the liver parenchyma. NAFLD comprises a wide spectrum of liver damage, ranging from simple macro-vesicular steatosis to steato-hepatitis, advanced fibrosis and cirrhosis. Subsets of NAFLD which progress to cirrhosis are being increasingly recognized as a major cause of liver related morbidity and mortality with the potential to progress to liver failure. Ludwig and colleagues [2] in 1980 originally coined the term nonalcoholic steatohepatitis, “NASH” to describe the histologic evidence suggestive of alcoholic hepatitis on liver biopsy (i.e., steatosis and lobular inflammation) but no history of alcohol abuse. Many of these patients were females (60%) and the majorities were obese (90%). Several other terms have been used to refer to this entity, including pseudo-alcoholic liver disease, alcohol-like hepatitis, diabetic hepatitis, non-alcoholic Laennec's disease, and steato-necrosis. However, seeing that the disease represents a spectrum of pathology, the umbrella term "NAFLD," first introduced in 1986, became the preferred one [3] .

The increased prevalence of fatty liver disease relates directly to the obesity epidemic seen in these populations. Most patients who come to medical attention with NAFLD are identified as a result of incidentally discovered elevated liver enzymes; Alanine transaminase (ALT), Aspartate transaminase (AST) and/or fatty liver on ultrasound examination. When patients are symptomatic, symptoms include fatigue or a vague right upper quadrant discomfort. Aminotransferases are only mildly (1.5–2 times the upper limit of normal) elevated, ALT is generally higher than AST. Recent studies have shown that many patients can have advanced fibrosis with NASH and even cirrhosis due to NASH with normal liver enzymes, indicating that the prevalence of the disease is likely to be even greater than was previously suspected [4].

The degree of liver fibrosis estimation helps to determine the prognosis and optimal treatment for fatty liver disease. Liver Biopsy is taken as the standard reference for the diagnosis and staging of fibrosis and is considered the gold standard in diagnosis and the only reliable tool for distinguishing NASH from simple steatosis and for grading and staging the disease, providing important information about severity of steatosis, lobular inflammation, hepatocellular ballooning, and degree of fibrosis [5]. However this procedure is invasive and associated with high risk of complications and significant sampling and observer error because of the evaluation of a very small volume of tissue sample which is only 1/50000 of the total volume, thus limiting the accuracy for determination of fibrosis stage of liver. Liver biopsy is also unpleasant for patients and usually requires hospitalization and for the adequate interpretation of the specimen requires a pathologist with expertise in hepato-pathology, which altogether makes it a costly and time-consuming procedure. In a well-designed study by Ratziu et al [6], the negative predictive value of a single biopsy for the diagnosis of NASH was calculated to be only 74%.

Hence several non-invasive methods of histological assessment including clinical, biochemical and radiological methods have been developed. Neven Baršić et al [7], worked on the overview and developments in non-invasive diagnosis of non-alcoholic fatty liver disease and concluded that even though, the gold standard still used in almost all of the studies is liver biopsy, but the question that remains is whether we are actually able to accurately assess the performance of non-invasive methods when the gold standard by itself has significant flaws. The study concludes of that there is a need for a new much efficient and a non-invasive tool for the diagnosis of NAFLD.

In this study we are discussing a review based study on a non-invasive, cost effective technique, without any radiation hazards, to measure the elastic property of liver tissue using ultrasound imaging modality called as sonoelastography in Indian population for assessment of disease severity and grading of nonalcoholic fatty liver disease.

MATERIALS AND METHODS:

The common methods for sonoelastography examination are as follows:

- The diagnosis of NAFLD is based on the clinical findings and routine ultrasound examination of the upper abdomen.
- The healthy controls can be selected based on the criteria ; age older than 18 years, no H/O alcohol intake, no known H/O diabetes, hypertension, hypothyroidism, Jaundice in the past, body mass index (BMI)<25kg/m^2, normal LFT, normal lipid profile, negative viral markers for Hepatitis B (HepB) and Hepatitis C (HepC) and normal liver on routine USG examination.
- The patients of NAFLD can select based on the criteria ; age older than 18 years, no H/O alcohol intake, No known H/O diabetes, hypertension, hypothyroidism, jaundice in the past, negative viral markers for HepB and HepC, fatty liver on routine USG examination
- Clinical profile of all the patients including BMI must be noted, Liver function tests and lipid profile can be done in all patients. Grading of fatty liver was done based on the USG findings.
- Sonoelastography can be performed on all the healthy controls and the patients and their values must be noted.
- Liver biopsy can be done as and when indication clinically.

<u>Technique of Sonoelastography</u>

Preparation of the patients:

Before starting the scan, procedure was explained to the patient in his/her vernacular language to allay any kind of fear and anxiety. A written consent about the explained details of investigation was taken.

Scanning Procedure:

Sonoelastography was performed on ultrasound. Shear wave elastography (SWE) of liver can be done using convex probe after making proper position of the patient and appropriate positioning of the US probe. Eight acquisitions can be performed by placing the SWE box at different areas of liver. The readings of liver stiffness and velocity must be noted in kilopascals (kPa) and metres/second (m/s) respectively. A median value may then be determined and used as a representative measurement of the liver elasticity. Findings of shear wave sonoelastography of healthy controls can be considered as normal values for the purpose of comparison with the values obtained in patients of NAFLD. The findings of shear wave elastography will then be correlated with clinical profile and laboratory investigations and with liver biopsy wherever done.

Discussion:

Imaging modalities frequently used in the diagnosis of NAFLD include ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI). While they are all very sensitive (80%-100%) and specific in detection of steatosis, none of them can effectively distinguish simple steatosis from NASH or determine the degree of fibrosis [8]. Ever since Hippocrates, physicians have used palpation to detect differences in tissue stiffness as an aid to diagnosis. Elastography depends on the same differences in mechanical properties between healthy and abnormal tissues but uses imaging to detect these differences at depths not reachable by manual palpation. Elastography techniques have been developed for both ultrasound and MR imaging. A major surge in development of ultrasonic methods and devices for elasticity imaging started in the late 1980s and early 1990s [9- 12]. Beginning in the late 1990s several laboratories developed an alternative approach for remote probing tissue elasticity using acoustic radiation force [13-15]. Acoustic radiation force is the time-average force exerted on an object by an acoustic wave.

Until recently, Elasticity Imaging was largely a research method used by a few select institutions having the special equipment needed to perform the studies. Since 2005 however, increasing numbers of mainstream manufacturers have added elastography to their ultrasound systems so that today the majority of manufacturers offer some sort of elastography or tissue stiffness imaging on their clinical systems. Now it is safe to say that elasticity imaging may be performed on virtually all types of focal and diffuse diseases. Transient Elastography (TE) uses an external actuator to provide a single cycle of low-frequency (typically around 50 Hz) vibration and ultrasound methods to track the resulting motion. This type of excitation generates four types of waves including a compression and shear wave in the medium. The compression and shear waves are separated in time because the longitudinal wave speed is, in most cases, much faster than the shear wave. Applying a sinusoidal excitation at low frequencies with a mechanical actuator with a small cylindrical footprint can cause biases due to wave diffraction from the cylindrical source. Using a transient excitation avoids these biases so that the shear wave can be separated from the compression wave and any reflected waves [16, 17] . TE has been used both as a one-dimensional (1D) measurement technique [17, 18] as well as a two-dimensional (2D) imaging technique [19]. The technique has been developed for measurement of stiffness in the liver in a product called Fibro Scan® manufactured by EchoSens [20]. TE has also been employed for measuring stiffness in phantoms, skeletal muscle, breast, skin, and blood clots. Shear Wave Elasticity Imaging (SWEI) was initially described theoretically by Sarvazyan et al. [21] and investigated experimentally by Nightingale and Trahey [22] and their combined work was a catalyst for many investigations and development of other techniques that followed. The use of modulated ultrasound was proposed to produce an acoustic radiation force imaging (ARFI) that would create shear waves that could be detected by optical, acoustic, ultrasound, or MRI methods. The radiation force acts as a "virtual finger" that may be used to palpate the organ from the inside, thereby replacing the physician's fingers on the surface of the body or organ.

In SWEI and ARFI imaging the radiation force is focused at a single location. An extension of these methods is to focus the radiation force in one location and then change the depth of the focal location so that the shear waves created from multiple focal locations constructively interfere to make a conical shear wave [23]. This method is called the Supersonic Shear Imaging (SSI) because the radiation force focal point moves at a rate that is faster than the speed of the shear wave in the medium, providing credence to the "supersonic" nomenclature. The shear wave created forms a kind of Mach cone and the Mach number of the excitation can be adjusted make the shear wave directionally oriented. Detection is accomplished by ultrafast real-time ultrasound imaging, and the data are displayed in kilopascals (kPa) and velocity in meter per second (m/s). This method has the advantage of being quantitative, reproducible, and operator independent. It is therefore suitable for monitoring changes over time. Nevertheless, MRI is more sensitive than ultrasound in detecting lesser degrees of hepatic steatosis, and new techniques in MRI are constantly being developed that provide additional data on different tissue parameters. One of them is magnetic resonance (MR) elastography, which estimates liver tissue stiffness by imaging the propagation of induced shear waves with a modified phase-contrast MR sequence. This technique was shown to have an excellent predictive value for excluding fibrosis, while sensitivity and specificity for discriminating between mild and more severe fibrosis was around 85% [24][25] . The future advances in MRI technology including hepatic flow parameters and diffusion-weighted MRI may hopefully provide more MR-based tools for liver fibrosis detection. However MRE may not be widely available for evaluating liver stiffness and its use as a screening tool may be time consuming and cost-prohibitive compared to ultrasound-based techniques.

Conclusion: On the basis of findings we can conclude that:

- A standard technique of liver sonoelastography can be established.
- Can determine the normal values of liver sonoelastography in our healthy controls.
- Can easily evaluate the role of sonoelastography of liver in patients of NAFLD.
- Easily compare the sonoelastography findings with the clinical profile, body mass index, liver function tests (LFT), lipid profile and wherever required with liver biopsy

In this review based study we can conclude that a non-invasive, cost effective technique, without any radiation hazards, called as sonoelastography in Indian population for assessment of disease severity and grading of nonalcoholic fatty liver disease can easily determined compared to other medical devices.

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