Validity of Ultrasound Shear Wave Elastography and Aminotransferase Platelet Ratio Index (APRI) in Liver Fibrosis

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Abstract

Background: Chronic progressive liver diseases cause liver fibrosis which end in result is decompensating liver failure. Liver fibrosis that results from these diseases can be reversed if diagnosed early. The current gold standard in the diagnosis of liver fibrosis is a liver biopsy preferably ultrasound guided, which is an invasive procedure with limitations and risks. Recent research has validated the use of shear wave ultrasound based liver elastography which is a non-invasive imaging based tool that has a sensitivity and specificity that almost parallels histological diagnosis from a liver biopsy. The staging of liver fibrosis at diagnosis uses a Metavir scoring system that has been adapted by elastography.

AIM: To assess the accuracy of point shear wave elastography with aminotransferase platelet ratio index score in the staging of liver fibrosis in chronic liver disease.

Materials and Methods: The study was carried out at Al Ameer Diagnostic Center of Radiology and Gastroenterology Center in Al Sadder Medical City in Al Najaf. During the period between November 2017 and July 2018, 62 patients each of them was examined by 2D point Shear Wave Elastography which is built in Ultrasound Machine Affinity 70 Philips, France with a multiband frequency convex probe. Liver function test with Liver biopsy was performed under ultrasound guidance from right liver lobe, under local xylocaine 2% injection with using 16 gauge co-axial automatic True cut biopsy needles.

Results: A total of 62 patients had been included in this study, 38 (61.29 %) were males and 24 (38.71%) were females with mean age 44.61± 14.92 years for all patients. Their Body Mass Index was 26.88 ±5.3 Gray scale ultrasound examination of the liver revealed that, the mean of cranio-caudal diameter of right lobe was 129.01± 11.6 mm. Regarding hepatic parenchyma texture, in 48 patients had normal texture, in 13 patients with coarse texture, heterogeneous texture seen in 1 patient. Fifty-five patients had regular hepatic surfaces and 7 patients with irregular surfaces. Portal vein mean transverse diameter in 58 patients was 12.08 ± 1.83 mm, in remaining 4 patients, the portal veins were occluded by thrombosis, portal vein mean velocity was 22.2 ± 5.2 cm/s. The mean of Liver Stiffness Measurement for the studied population was 12. 5 ± 2.07 (mean± Standard Diffusion). Aminotransferase Platelet Ratio Index mean score for the studied population was 1. 2 ± 0.8. These patients were sub grouped in five categories according to Liver Stiffness Measurement, 8 patients in grade F0 (< 4.6), 14 patients grade F1 (4.6-5.6), 10 patients were F2 (5.7-7.0), 15 patients were in grade F3 (7.1-12) and 15 patients were in grade F4 (>12). While according to histopathological examination, the studied population were categorized as 14 patients F0, 16 patients were F1, 9 patents F2, 1 patients F3 and 12 in F4. Regarding the Aminotransferase Platelet Ratio Index score the studied patients were classified as grade 0 (<0.5) 8 patients, grade 1,2&3 (0.5-1-1.5) 42 patients and grade 4 (>1.5) 12 patients. Out of 62 patients enrolled in this study twelve patients were categorized by Aminotransferase Platelet Ratio Index score as F4 with cirrhosis, ten of them were positive in histopathology as F4 and two were negative, while 50 patients were categorized as F0-3 with no cirrhosis, 48 patients were positive in histopathological examination as F0-3, and 2 patients were false negative proved by histopathology as F4 with cirrhosis, so the Aminotransferase Platelet Ratio Index Score Sensitivity was 83.3%, Specificity was 96%, Positive Predictive Value was 93.5, Negative Predictive value was 96% and the Accuracy was 93.5%.

Conclusions

1- point Shear Wave elastography is a useful tool to screen for liver fibrosis in the general population during a conventional ultrasound examination, especially when laboratory tests and ultrasound examination are negative despite the potential underlying fibrosis.

2- Gray scale ultrasonography alone is insufficient imaging modality for full assessment of chronic liver disease.

3- A simple index like Aminotransferase Platelet Ratio Index, consisting of 2 readily available laboratory results (Aspartame aminotransferase Test level and platelet count), can predict cirrhosis with high degree of accuracy. Besides being non-invasive, it can be determined at the bedside. It can also be of use in areas where facilities for liver biopsy and advanced imaging techniques are not available.

KEY WORDS: Shear wave elastography, liver fibrosis, Aminotransferase Platelet Ratio Index and Liver biopsy.
Introduction and review of literatures

Anatomy

The normal liver surface is smooth and brown color, in adult it is about 2% of all body weight. The midclavicular line (MCL) averages 10-12.5 cm, in cranio caudal length (CCL) of a liver is about 15.5-16 cm that is longer than in the midclavicular line which considered as enlarged if measured in this manner. The spleen lies to the left of the liver; the normal adult splenic length upper limit is usually around 12-13 cm. The liver received blood supply from two sources; from portal vein about 80% that drains the spleen and intestines; the remaining is 20%, while the hepatic artery delivers the oxygenated blood (1). The union between splenic vein and superior mesenteric vein formed the portal vein. The celiac artery gives common hepatic artery, left gastric artery and splenic artery. In some people the left hepatic artery replaced by branch of left gastric artery while the right hepatic artery is replaced by branch from proximal superior mesenteric artery (2). The segmental anatomy of liver is based on the distribution of the portal and hepatic veins between two lobes. Each lobe contains 4 segments, so they are eight in depended functional segment each of them has its own portal pedicle contain branches from hepatic artery, portal vein and bile duct. The segments are numbered on the left lobe counterclockwise I-IV while V-VIII in the right lobe figure (1.1)

Pathology of Chronic Liver Disease

The liver fibrosis is the excessive accumulation of extracellular matrix (ECM) proteins including collagen that occurs in most types of chronic liver diseases (5,6). The hepatic parenchyma is composed of epithelial cells (hepatocytes), endothelial cells, and resident non parenchyma cells, including hepatic stellate cells (HSCs) and Kuepfer cells (KC) (7) (figure 1.2). The micro vascular unit of liver called sinusoid, the sub endothelial space of Disse separated hepatocytes from endothelial that contain fenestration of pores. This space helps metabolic exchange between
hepatocytes and the blood stream. Capillarization of the sinusoids: is the accumulation of EMG in the space of Disse that normal fenestration loss its normal shape lead to impairment of metabolic exchange between hepatocytes and portal venous flow (figure 1.3).

Figure 1.2: Sinusoids are separated from hepatocytes by a low-density basement membrane–like matrix confined to the space of Disse, which ensures metabolic exchange. Upon injury, the HSCs become activated and secrete large amounts of extracellular matrix (ECM), resulting in progressive thickening of the septa (7).

Figure 1.3. Deposition of ECM in the space of Disse leads to the loss of both endothelial fenestrations and hepatocytes microvilli, which results in both the impairment of normal bidirectional metabolic exchange between portal venous flow and hepatocytes and the development of portal hypertension (7). The more accumulation of ECM proteins lead to damage the liver architecture by forming a fibrous scar, and the development of regenerating hepatocytes nodules defines cirrhosis. That led to hepatocellular dysfunction and increased intra hepatic resistance to blood flow, which result a portal hypertension (8). So by the time the increment of liver fibrosis results in cirrhosis, liver failure, and portal hypertension and often requires liver transplantation (6). The (METAVIR) score. This score ranges from F0 to F4 for fibrosis (F0: no fibrosis, F1: portal fibrosis without septa, F2: few septa, F3: numerous septa without cirrhosis and F4: cirrhosis) and from A0 to A3 for activity (A0: none, A1: mild, A2: moderate and A3: severe) (9).

The main causes of liver fibrosis:
1- Hepatitis Viruses
2- Autoimmune Hepatitis
3- Liver Steatosis
4- Non-Alcoholic Fatty Liver Disease (NAFLD)
5- Alcohol-Induced Liver Disease

Methods of Diagnosis of Liver Diseases
Liver Multidetector CT
The normal liver parenchyma is homogeneous and its attenuation about 55-65 HU at unenhanced multidetector CT, while during attenuation it will be more than spleen by about 10 HU. The CT scans were performed with helical acquisition on 16- or 64-slice multidetector patients received IV contrast late arterial and venous, it can differentiate multiple liver disease: liver nodules ,superficial modularity, varices, heterogeneous enhancement, , relative enlargement of the left and caudate lobes with right lobe atrophy and areas of confluent fibrosis like in (figure1.4)(10,11). The irregularity in the contour of the liver surface was called Superficial modularity, during late arterial phase imaging the liver nodules were defined an intense focal areas of enhancement, while the heterogeneous and diffuse patchy enhancement seen during
portal venous phase imaging\(^{(12)}\). Optical analysis of CT images of the liver (Fibro-CT) has been used to assess fibrosis in patients with chronic hepatitis C virus (HCV) infection \(^{(13)}\). The use of fibro-CT is time consuming and more expensive than the noninvasive serum markers \(^{(14)}\).

![Liver abnormalities identified on CT scan.](image1.png)

**Figure 1.4:** Liver abnormalities identified on CT scan. (A) Superficial modularity ;(B) heterogeneous enhancement ;(C) enhancing liver nodules (arrow); (D) areas of confluent fibrosis (arrowhead) \(^{(12)}\).

### 1.3.2 Magnetic Resonance Imaging of Liver

Many MRI based techniques have been evaluated for assessing liver fibrosis like: diffusion weighted imaging (DWI), perfusion MRI, MR Spectroscopy (MRS) and MRElastography (MRE) \(^{(15)}\), \(^{(16)}\). This provides quantitative maps of tissue stiffness over wide hepatic region (figure 1.5), MRE requires less than a minute of acquisition time. Subsequently, MRE in patients with fat content or liver varices, hepatic iron overload is the most frequent reason for technical failure in MRE by decrease hepatic signal intensity in gradient echo based MRE sequences to unacceptably low levels \(^{(18,19)}\).

![MRI and MRE a: A mechanical waves generate in the tissues of interest from source of vibration placed on the surface of the body b: A special MRE pulse sequence with synchronized motion encoding gradients.](image2.png)

**Figure 1.5:** MRI and MRE a: A mechanical waves generate in the tissues of interest from source of vibration placed on the surface of the body b: A special MRE pulse sequence with synchronized motion encoding gradients. The wavelength of the shear waves is shorter in softer tissues and longer in stiffer tissue c: The wave images are then automatically processed with an “inversion algorithm” to create quantitative images depicting the stiffness of tissue \(^{(17)}\).

### 1.3.3 Ultrasonography

Liver is difficult to image, these difficult areas are the left tip of the lateral segment of the left lobe, the superficial liver above the costal margin and the ventral sub diaphragmatic regions. The liver is starting to exam with gray scale 3–7 MHz curved probe and the patient in the supine and left lateral deceits positions, the surface liver of the left lobe **should** be evaluated for modularity with 5-12 MHz linear array transducer because it is more ventral but in obese patient high-frequency curved linear transducers is used in figure (1.6).

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Ultrasound Elastography imaging
There is interconnection between the elasticity of the tissue and its pathological states that help the physician to assess tissue health manually that is different from physician to another, they found the healthy liver is more softer than cirrhotic liver and they searching for stiff nodules in the testicular and breast cancers, so it must be found technique that the measurement of elasticity not depended on the physician but on tissue mechanical properties that depend on elasticity called Elastography. The elasticity of normal and malignant liver tissue has been quantified, the degree of liver fibrosis has been correlate with tissue elasticity (21,22,23).

1.3.3.1.1 Principles of Ultrasound Elastography
The term of technique that describes an ultrasound based imaging is called"Elastography" and this was developed by Ophir et al (24,25). Local tissue displacement can be estimated by effect of (palpation or compression) - which we called quasi-static tissue deformation and comparing sets of ultrasound data. Many types of new Elastography have been developed either using ultrasound or magnetic resonance imaging (26, 27,28).

The elasticity can be measured by:
1. Quasi-static or dynamic physical stress that produce tissue displacement.
2. Radiofrequnce ultrasound data assess quasi static or dynamic displacement.
3. Estimate an elasticity parameter by using the estimated quasi-static or dynamic displacement data like share wave speed measure in meter per second, displacement amplitude in micrometer, share modulus and young’s modulus (which is the physical parameter equal to the stiffness) in Kilo-Pascal, and strain measured by percent. The Young’s modulus(E) display modification among different biological tissues that help to differentiate tissues with a contrast (29). also it characterizes tissue stiffens exactly quantitative a clinician’s palpation, so that the relation between palpation and Elastography is called (palpation imaging) like in liver fibrosis staging or in breast tumor.

Quasi –Static Elastography
Quasi static Elastography match pre and post compression Elastography to chart, many ways of compressions like in this figure (1.7) below

Figure 1.7: Commonly used tissue excitation methods in Elastography imaging (a) for quasi-static compression, compression device may be used to compress the tissue, but the ultrasound
Transducer is also commonly used. (b) Continuous or (c) transient tissue excitation typically requires a vibration source. (d) Acoustic radiation force is also used to perturb tissue and is generally a transient event. It is often generated with the ultrasound transducer, which is also used to track tissue displacement. The Young's modulus is given via the Hooke's law (\( = E \)), which links stress (force per unit area) and strain (proportional deformation) in a purely elastic medium. We can use ultrasound transducer as a compression device by applying freehand compression as a constant stress applied to the tissue, when we used freehand motion can be described as low frequency excitation, while arterial motion, heart motion and respiratory motion can be called physiological motion which is used like natural compression source. Tissue strain can be evaluated from data of pre and post radiofrecoancy compression, at the beginning the strain estimation and displacement estimation algorithm used 1D but then used 2D and full 3D. Axial share strain it is another type of Elastography that use to mark the power of bonding between the lesion and surrounding background like type of malignant versus benign.

**Dynamic Elastography**

In dynamic methods the time-varying force which applied to the tissue, it can either wavering force with a fixed frequency or may be a short transient mechanical force, so in a solid body spread as mechanical waves either like shear waves or longitudinal(compression) waves like in figure (1.8).

![fig1](image.png)

Figure 1.8 (a): the longitudinal wave (P) spreads by successive volume variations of the medium. The displacement of the medium \( u \) is parallel to its propagation direction with a speed of \( V_L \). The ultrasounds used in ultrasonography are longitudinal waves. Sound is also a longitudinal wave in the range of audible frequencies, (b): the shear wave (S) spreads by successive movements that are perpendicular to the direction of propagation with a speed of \( V_S \). Shear waves, which are generated only at low frequencies (10 Hz to 2000 Hz) because absorption at higher frequencies, slowly spread with speed about (1-50 m/s) is directly related to the shear modulus medium (\( = V_S^2 \)) in density of the area about (1000 kg/m3) in biological tissues, which are almost incompressible.

The external mechanical excitation is common process to produce waves in tissue and this either (transient or continuous), in continuous approach the standing and reflecting wave may cause biases in elasticity estimation. But when we use transient pulse we can reduce this effect of biases by produce share waves that spread from surface body to the tissue of interest and both these methods are illustrated in figure (6).
Techniques of Ultrasound Elastography

A- Mechanical Stimuli

A-1. Strain Imaging
Tissue pathology can be detecting in different region by strain imaging that match data of pre and post compression to map tissue strain, which applied in common application like liver, thyroid, breast and prostate (40), (41), (42). Strain can be estimated by physiological motions like cardiac strain from cardiac motion, arterial strain measuring by intravascular ultrasound and superficial vessels like carotid artery measuring by conventional superficial probe (43).

A-2. Sonoelastography
Tissue elasticity can be measured by Sonoelastography by hunt share waves generated from continues external tracking vibration produce from Doppler tracking technique (44), (45). That used two vibration sources at a little make up frequencies called (crawling waves) that much speed slower than share waves. Sonoelastography is success in liver and prostate and characterizing muscle elasticity in vivo (46).

A-3. 1D and 2D Transient Elastography
The probe of 1D transient Elastography was first developed in 1995 at the Institute Langev (39). It depends on producing transient impulse on the medium and register the shear wave that transmit within the medium by using an ultrasound transducer.

Figure 1.9: The vibrator gives a low frequency pulse (adjustable from 10 Hz to 500 Hz) in the medium, creating, among others, a shear wave (30).

At the beginning, the forehead of the transducer working as a compressor gives a little mechanical impulse on the surface of medium, which generates a spherical compression wave in addition a spherical shear as in figure (1.9) (39), the transducer of ultrasound that placed on the vibrator give subsequent, by axial interconnection of the ultrasound speckle and more than 1000 times per second, the propagation of the shear wave depending on the depth over time. Then we can understand the speed of the shear wave and thus the Young’s modulus of the medium by considering the medium non viscous and homogeneous. At first this process designed for control the quality in the food industry, then applied to the medical field (47), since 2001 the 1D transient Elastography, known as FibroScan. This appliance gives the expressing quantity of hepatic (or splenic) fibrosis by granting total score of elasticity at 50 Hz in depth (from 20 to 60 mm). In chronic liver disease the 1D transient Elastography has become a reference technique, as it is a non-invasive method that decrease more than fifty percent of liver biopsies (48), (49). The 2D was extended from the 1D transient Elastography technique at the “Institute Langev in” in 1997, was extended to, allowing the which permit the originality of elasticity maps of biological tissues. It permits powerful fine data obtained with a frame rate of more than five thousand images per second. A vibrator was fixed to the ultrasound imaging array, which is then used as an impact or to generate a quasi-plane shear wave (Fig.1.10) (30).
Figure 1.10: The ultrasound array, fixed on a vibrator, gives (around 50 Hz) which is a low frequency shock in the medium, the shear wave produced on the borders of the array overlap within the imaging plane as a quasi-plane wave increase in the depth; 2: To follow the shear wave that is spread through the medium the ultrasound will close into an ultrafast imaging mode.

The wave equation is reversed to improve a map of Young’s modulus at the moment that the movie of the spread of shear wave is reconstructed, the first tests were encouraging in 2003 with volunteers at Institute Curie, but the device was huge, weighty and difficult to use in practice. In clinical scanner the Real-time 1D & 2D transient elastography have been implemented.

A-4 Needle Based Approaches
Some used needles as vibration source or as mechanical compression particularly through athermal ablation treatment when needle is inserted into pathological area and by heating or freezing the normal tissue in the surrounding will be destroied which causes the needle bind to the tissue, so with the attachment of the needle through the ablation area the tissue may be locally vibrated or compressed. A strain imaging technique called Electrode displacement elastography (EDE) that uses the ablation needle as quasi-static compression device. From pre and post compression data the strain imaging will generate and used to delineate a ablation zones this show in ex vivo thermal ablation and phantom. another technique of ablation needle is continous vibration that used in liver tissue and phantom.

B- Acoustic Radiation Force
B-1. Acoustic Radiation Force Impulse (ARFI) Imaging
The technique that make focused acoustic beam to pushed the tissue and focused tracking pulses which are subsequently called Acoustic radiation force impulse (ARFI) that used to capture tissue response till fully recover, so it is uses, high intensity acoustic pulses, short-duration to mechanically excite the tissue. with another frequent pushes from main component of the transducer and maximum displacement is chart (mapped) to create a 2D elasticity image. another value can be mapped like recovery time and time to peak displacement, parallel receive beam is used to increase data and in the same time decrease tissue heating by receive data from many sites neighboring push location. finally, we can say that shear waves are radiation force excitations create localized tissue displacements, which velocity (SWV) of spread can be assessed in a region of interest (ROI) identical to a cylinder, 0.5 cm long and 0.4 cm wide 5.5 cm under the skin. at same ultrasound probe both the high-energy pulse and the conventional ultrasound pulse are generated and the outcome in m/s. ARFI is integrated into a conventional ultrasound system and preliminary results have shown that even severe obesity is not a limitation for this technique. Many applications of ARFI confirm in liver, breast, cardiac, gastrointestinal and prostate. Tracking the shear wave that generated by the push at the lateral offset from the push location with focused serially scanned ultrasound called Quantitative ARFI. Figure (1.11).
Figure (1.11): Comparison of the ARFI imaging techniques, on the left focused acoustic pulse at transducer location that filled the blank with ARFI pushes tissue with long duration. The result is tissue tracking through the time that result(peak)maximum, recovery time and time to peak displacement. On the right the quantitative ARFI push the tissue but track the shear wave produce by the push with subset elements at lateral offset from the push location to measure tissue shear wave speed which proportional to the tissue shear modulus. Note the diagram depicts tracking right of the push location, but the shear wave could also be tracked left to the push (25).

The classify the thyroid and breast lesion and grading of liver have been used by Quantitative ARFI (60).

B-2 Supersonic Share Imaging (SSI)
The Supersonic Shear Imaging technique is limitations of 2D elasto graph technique: (first acoustic radiation force and second ultrasound ultrafast imaging).

First: Mach cone
At different depths the ultrasound beams are successively focused. For each focal beam different spherical waves generated and interfere like a Mach cone, in which the generated shear waves more slowly than the source propagate and produce a quasi-plane wave front in the imaging plane. The use of constructive interfaces makes the signal to noise ratio of the displacement area by increasing e the amplitude of the wave. At the end only one Mach cone permit blooming about the entire medium with one plane shear wave, as in figure (1.12).

Second: ultrafast imaging
Complete acquisition all instantly. Ultrafast imaging permeates survey the entire imaging plane with very good temporary resolution in one single acquisition, typically 5000 images per second frame rate, and more than 30,000 images per second as in the eye or the peripheral arteries, so there is no need to renew the acquisition several times. This makes imaging in real-time easier and improve image quality very rapidly (30).

SSI have many applications in liver, thyroid, breast and prostate. It used to staging liver fibrosis, myocardial and arterial elasticity (61, 62).

B-3. Vibro Acoustography
The acoustic response of an object that is vibrating with radiation force called vibroacoustography (63). Little different in frequency of two ultrasound beams that are focus at the same special location, acoustic emission and elasticity of the object is recorded with hydrophone. The process is repeated during imaging due to the focus position is moving. The useful thing of the vibroacoustography is the imaging is not speckle like ultrasound imaging of
traditional B-mode. it applications in liver, thyroid, breast, prostate, calcified arteries and fractures of bones.

**Ultrasound Elastography Clinical Applications**

**A- Breast**

Strain imaging success to differentiate between malignant and benign tumors, tumor width measure by Elastography is greater than it actually measures by sonography or gross pathology, this is due to the stiffness in the periphery of the tumor as a result of desmoplastic reaction in periphery that not change tissue echogenic characteristics \(^{(64)}\).

**B- Liver**

Quantitative Elastography is noninvasive method with much larger area than biopsy for staging of liver fibrosis. Several quantitative Elastography for staging are used like:

1. 1D transient Elastography on FibroScan \(^{(48)}\).
2. A meta-analysis staging of liver (fibrosis, sever fibrosis and cirrhosis) \(^{(65)}\).
3. Quantitative ARFI assess normal tissue and staging of fibrosis \(^{(66)}\).
4. SSI quantifies normal and fibrotic tissue elasticity \(^{(67)}\).

But fatty patient limits this technique because fat layer leads to signal attenuation, also all these types can detect, delineate and classify hepatic tumors

**C- Prostate**

Elastography is good method in malignant prostate because low positive biopsy rate and the complication of biopsy, the malignant tumor is stiff but the contrast between normal and malignant tissue is low that made detection of malignancy is a challenge, also it may give false positive in area of calcification because it looks stiffness like malignancy. strain image is good but compression on scrotal lead to artifact so must balloon to decrease compression artifact and decrease operator depended artifact \(^{(68)}\).

**D- Cardiac and Vascular Application**

Speckle tracking or Doppler techniques is used to detect cardiac wall and the myocardial function quantify by Elastography. The detection the differences of stiffness in stiff fibrous area and soft lipid area we used ARFI technique \(^{(69)}\).

**E- Musculoskeletal Application**

Tendons can be visualized by strain imaging. Achilles tendon is more stiffness than normal tissue around it but when there is pathology like fibrosis or tumor lead more stiffness in tissue, while tendinopathy lead tissue to be more soften \(^{(70)}\). Like in (tennis elbow) lateral epicondylitis or Achilles tendinopathy. 1D used to measure the increase in elasticity of biceps tendon during increase of muscle capacity \(^{(71)}\).

**F- Other Applications**

Strain imaging and ARFI both show that malignant thyroid nodule is more stiffness than normal thyroid tissue and also more than benign nodule \(^{(72)}\). SSI differentiated between benign and malignancy thyroid tumors also the elasticity of the thyroid tissue. Also Elastography used in graft rejection FibroScan in renal and liver transplant. SSI used in poor attachment between pathological changes after renal transplant and tissue elasticity \(^{(73)}\).
Liver Biopsy

Complications of liver biopsy are rare but potentially lethal. The majority of complications (60%) occur within two hours, and 96% occur within 24 hours following the procedure. Approximately 2–3% of patients undergoing liver biopsy require hospitalization for the management of an adverse event. Thirty percent of patients experience significant pain during the procedure. Significant bleeding after a liver biopsy occurs in 1–2 out of 100 patients who are biopsied. Bleeding usually becomes apparent within three to four hours. Intraperitoneal hemorrhage is the most serious consequence of bleeding. Fatal complications have been reported in up to 0.01–0.3% of biopsied patients. Biopsy results show significant variability (up to 40% for fibrosis diagnosis) which can lead to a wrong diagnosis. The result depends on the representatively of the punctured sample. Only 5% of patients at risk of fibrosis have liver biopsy. In 2002, the consensus conferences in France and in the USA raised the possibility of treating patients with chronic hepatitis without liver biopsy. Liver biopsy will likely remain particularly important in the diagnosis of unexplained liver disease. Non-invasive tests for liver fibrosis in alcoholic, nonalcoholic and viral liver diseases are likely to become more widely used.

AIM: To assess the accuracy of point shear wave elastography (pSWE) and aminotransferase platelet ratio index (APRI) score in the staging of liver fibrosis in chronic liver disease.

Patients and Methods.

This cross sectional study was carried out at Al Ameer Diagnostic Center of Radiology and Gastroenterology Center in Al Sadder Medical City in Al Najaf. During the period between November 2017 and July 2018, all patients gave their written informed consent for taking part in this study. The study was approved by Ethical Committee of Faculty of medicine, Kufa University. It included 100 patients that were referred for ultrasound liver FibroScan for assessment of liver stiffness; Patients were referred for FibroScan because of known or suspected chronic hepatic disease.

Patients

Sixty-two from One hundred consecutive patients were referred to liver FibroScan, 60 were male and 40 were female with their age between 25-78 years.

Inclusion Criteria

Inclusion criteria were the presence or suspicion of chronic hepatic diseases.

Exclusion Criteria:

1- Liver sepsis.
2- Venous congestion.
3- Cholestasis.
4- Infiltrative neoplastic process.
5- Recent meal ingestion less than 6hrs.
6- Moderate to large ascites.
7- Bleeding tendency.
8- Lack one of liver biopsy, APRI score or SWE.

Methods

Liverfibroscan: liver stiffness measurement was performed by 2-D Point Shear Wave Elastography which build in Ultrasound Machine Affinity 70 Philips, France with a multiband frequency convex probe (Fig.2.1)
Liver Stiffness Measurements

Measurements were performed in the right lobe of the liver through the intercostals spaces on patients lying in the supine position with the right arm in maximal abduction. The probe was covered with coupling gel and placed on the skin. Firstly, a routine ultrasound studies to assess liver dimensions including cranio-caudal diameter, liver echogenicity and outline of the liver surface. Portal vein diameter measurement at I.V.C level with assessment of its blood flow direction and velocity also performed. The spleen was also examined, concentrating on long axis diameter measurement. LSM was performed with a real time sonography and point Shear Wave Elastography (pSWE) technique. After general sonography examination was completed, the patient was asked to stop breathing, not to take deep inspiration, just hold his breath, the Scan gram box cited in the right liver lobe within 60 mm thickness away from the skin, avoiding large vascular structures or bile duct. Once the area of measurement had been located, the operator asked patient to hold breathing and a bottom of Scan gram pressed while the probe fixed in the intercostals space to begin an acquisition. The measurement depth was between 25 and 45 mm. Ten successful acquisitions were performed on each patient. The success rate was calculated as the ratio of the number of successful acquisitions over the total number of acquisitions. The average value was kept as representative of the liver stiffness. The entire examination time was 5-10 minutes. Only results of LSM obtained with 10 successful acquisitions and a success rate of at least 60% and the IQR/median equal or less than 30% were considered reliable. Interpretation of liver fibrosis by shear wave Elastography in kPa divided the entity into no fibrosis (F0), mild fibrosis (F1), severe fibrosis (F2), significant fibrosis (F3) and cirrhosis (F4). Automatic average value generated by the ultrasound software was used to establish the elastography grade as follows: F0 < 4.6, F1 = 4.6-5.6, F2 = 5.7-7.0, F3 = 7.1-12.0 and F4 > 12 (82), (83), (84).

Laboratory Tests

Liver function test comprised of parameters like SGOT, SGPT, Alkaline phosphates, and serum bilirubin, performed using a fully ROCHE COBAS C111 Auto Biochemical Analyzer. Platelet count was determined by the fully automatic mindery BC-5000 Auto Hematology Analyzer and Reagent.

We concentrated on the APRI Score, calculated as follow; (aspartate aminotrans -ferase of the patient/upper normal limit of AST) / platelet count (10^9/l) × 100). The upper normal limit of AST in male was 40 while in female was 30(85).

APRI score of < 0.5 was graded as F0, 0.5-1.5 as F1-3 and > 1.5 as F4. The corresponding histology grade was assessed (86), (87).

Liver Histology and Quantification of Liver Fibrosis

Liver biopsy was performed under ultrasound guidance from right liver lobe, under local xylocain 2% injection with using 16 gauge co-axial automatic True cut biopsy needle (fig.2-4), at least three pieces of tissue each one 20 mm length, the patients were kept under observation for two hours. The specimens were fixed in formalin and send for histopathological assessment, by experienced hepatopathologists, blindly from the results of LSM and APRI score. Liver fibrosis and necro-inflammatory activity were evaluated semi-quantitatively according to the METAVIR scoring system (88).

Fibrosis was staged on a 0-4 scale: F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis and few septa; F3, numerous septa without cirrhosis; and F4, cirrhosis.
**Statistical analysis**
Statistical analysis was done using SPSS version 20 numerical data expressed as mean +/-SD. Categorical data expressed as frequencies and percentages Independent t test for comparison of mean of 2 groups Chi square for comparison of categorical Variable ROC curve for selecting cutoff for elastogram P value equal or less than 0.05 was regarded as significant.

**Results**
Out of 100 patients 38 patients were excluded from the study for different causes, 3 of patients had ascites, 2 of patients had bleeding tendency, 3 patients had liver sepsis, 4 patients’ venous congestion, 5 patients had cholestasis, 5 patients had infiltrative neoplastic proses, 1 patients resent meal ingestion, 11 patients refused biopsy, 1 of patients lack LSM and 3 patient lack APRI. Remaining 62 patient were enrolled in the study, 38 (61.29 %) were males and 24 (38.71%) were females with mean age 44.61± 14.92 years for all patients. Their BMI was 26.88 ±5.3 (Fig.3.1).
Table 3.1: Illustrate History of the Studied Population

<table>
<thead>
<tr>
<th>History</th>
<th>Cause</th>
<th>No.</th>
<th>%</th>
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<tbody>
<tr>
<td>HBV</td>
<td></td>
<td>18</td>
<td>29</td>
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<tr>
<td>HCV</td>
<td></td>
<td>7</td>
<td>11.3</td>
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<tr>
<td>HBV+HCV</td>
<td></td>
<td>2</td>
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<td>Auto-immune</td>
<td></td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>NASH+Cirrhosis</td>
<td></td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td>31</td>
<td>50</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>62</td>
<td>100%</td>
</tr>
</tbody>
</table>

(NASH= NON ALCOHOLIC STEATOHEPATITIS)

Gray scale ultrasound examination of the liver revealed that, the mean of cranio-caudal diameter of right lobe was 129.01±11.6 mm. Regarding hepatic parenchymal texture, in 48 patients had normal texture, in 13 patients with coarse texture, heterogeneous texture seen in 1 patient.

Fifty-five patients had regular hepatic surfaces and 7 patients with irregular surfaces. portal vein mean transverse diameter in 58 patients was $12.08 \pm 1.83$ mm, in remaining 4 patients, the portal veins were occluded by thrombosis. portal vein mean velocity was $22.2 \pm 5.2$ cm/s. 
The spleen was assessed by gray scale ultrasound concentrated on the long axis diameter, the
mean diameter was 127.6 ± 29.7 mm.
The mean of LSM for the studied population was 12.5 ± 2.07 (mean ± SD) APRI mean score for the studied population was 1.2 ± 0.8 (Table 3.2).

Table 3-2: Gray Scale Ultrasound finding of the Liver and Spleen

<table>
<thead>
<tr>
<th>Ultrasound finding</th>
<th>No</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spleen long axis</td>
<td>62</td>
<td>127.6 ± 29.7 mm</td>
</tr>
<tr>
<td>Portal vein diameter</td>
<td>58</td>
<td>12.08 ± 1.83 mm</td>
</tr>
<tr>
<td>Portal vein velocity</td>
<td>58</td>
<td>22.2 ± 5.2 cm/s</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCD</td>
<td>62</td>
<td>129.01 ± 11.6 mm</td>
</tr>
<tr>
<td>Texture echogenicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal texture</td>
<td>48</td>
<td>77.42</td>
</tr>
<tr>
<td>Coarse</td>
<td>13</td>
<td>21</td>
</tr>
<tr>
<td>Heterogeneous</td>
<td>1</td>
<td>1.6</td>
</tr>
<tr>
<td>Regular surface</td>
<td>55</td>
<td>88.7</td>
</tr>
<tr>
<td>Irregular surface</td>
<td>7</td>
<td>11.3</td>
</tr>
</tbody>
</table>

Regarding 2D ultrasound pSWE for the 62 patients, these patients were sub grouped in five categories according to LSM, 8 in grade F0 (LSM < 4.6), 14 patients grade F1 (LSM 4.6-5.6), 10 patients were F2 (LSM 5.7-7.0), 15 patients were in grade F3 (LSM 7.1-12) and 15 patients were in grade F4 (LSM >12). While according to histopathological examination, the studied population were categorized as 14 patients F0, 16 patients were F1, 9 patients F2, 1 1 patients F3 and 12 in F4. Regarding the APRI score the studied patients were classified as grade 0 (<0.5) 8 patients, grade 1-3 (0.5-1.5) 42 patients and grade 4 (>1.5) 12 patients (Table 3.3), (Fig.3-3, 3-4).

Table 3.3: point Shear Wave Elastography, Aspartate Aminotransferase /platelet count score and histopathological groups

<table>
<thead>
<tr>
<th>Grade</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PSWEx grades</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F0</td>
<td>8</td>
<td>12.9</td>
</tr>
<tr>
<td>F1</td>
<td>14</td>
<td>22.6</td>
</tr>
<tr>
<td>F2</td>
<td>10</td>
<td>16.1</td>
</tr>
<tr>
<td>F3</td>
<td>15</td>
<td>24.2</td>
</tr>
<tr>
<td>F4</td>
<td>15</td>
<td>24.2</td>
</tr>
<tr>
<td><strong>Histological grades</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F0</td>
<td>14</td>
<td>22.6</td>
</tr>
<tr>
<td>F1</td>
<td>16</td>
<td>25.8</td>
</tr>
<tr>
<td>F2</td>
<td>9</td>
<td>14.5</td>
</tr>
<tr>
<td>F3</td>
<td>11</td>
<td>17.7</td>
</tr>
<tr>
<td>F4</td>
<td>12</td>
<td>19.4</td>
</tr>
<tr>
<td><strong>APRI grades</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F0</td>
<td>8</td>
<td>12.9</td>
</tr>
<tr>
<td>F1-3</td>
<td>42</td>
<td>67.7</td>
</tr>
<tr>
<td>F4</td>
<td>12</td>
<td>19.4</td>
</tr>
</tbody>
</table>
Fig 3-3: comparison of LSM mean ± SE according to elastography grading

Fig 3-4: classification of patients according to histopathological grades

Fig.3-5 Receiver Operator Curve for F4 vs F0-3 LSM and APRI score
Comparison of F4 vs F0-3 LSM, the area under the curve was 0.986 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.962 while the upper bound was 1.0. For the APRI score the area under the curve was 0.959 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.913 and the upper bound was 1.0. Cut off value for LSM 13.9 give 100% sensitivity and 96% specificity. Cut off value 1.35 for the APRI score gives 91.7% sensitivity and 84.9% specificity (table 3-4).
Table 3-4: Area Under the Curve in comparism of F4vs F0-3 of LMS and APRI score

<table>
<thead>
<tr>
<th>Variable(s)</th>
<th>Area</th>
<th>Std. Error</th>
<th>P value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>LSM</td>
<td>.986</td>
<td>.012</td>
<td>.0001</td>
<td>.962</td>
</tr>
<tr>
<td>APRI</td>
<td>.959</td>
<td>.024</td>
<td>.0001</td>
<td>.913</td>
</tr>
</tbody>
</table>

Comparison of F3-4 vs F0-2 LSM , the area under the curve was 0.99 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.974 while the upper bound was 1.0. For the APRI score the area under the curve was 0.948 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.90 and the upper bound was 0.99. Cut off value for LSM 7.6 gives 95.8% sensitivity and 92.7% specificity. Cut off value 1.15 for the APRI score gives 91.7% sensitivity and 82.9% specificity (table 3-5),(Fig 3-6).

Comparison of F2-4 vs F0-1 LSM , the area under the curve was 0.98 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.956 while the upper bound was 1.0. For the APRI score the area under the curve was 0.931 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.87 and the upper bound was 0.03.

Table 3-5: Area Under the Curve in comparison of F3-4 vs F0-2 of LMS and APRI score

<table>
<thead>
<tr>
<th>Variable(s)</th>
<th>Area</th>
<th>Std. Error</th>
<th>P value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>LSM</td>
<td>.990</td>
<td>.008</td>
<td>.0001</td>
<td>.974</td>
</tr>
<tr>
<td>APRI</td>
<td>.948</td>
<td>.024</td>
<td>.0001</td>
<td>.900</td>
</tr>
</tbody>
</table>

Cut off value for LSM 6.8 gives 93.9% sensitivity and 90.6% specificity. Cut off value 0.75 for the APRI score gives 90.9% sensitivity and 75% specificity (table 3-6), (Fig.3-7).
Out of 62 patients enrolled in this study twelve patients were categorized by LSM score as F4 with cirrhosis, all of them were positive in histopathology as F4 and zero were negative. While 50 patients were categorized as F0-3 with no cirrhosis, 47 patients were positive in histopathological examination as F0-3, and 3 patients were false negative proved by histopathology as F4 with cirrhosis, so the LSM score Sensitivity was 100%, Specificity was 94%, PPV was 80%, NPP was 100% and the Accuracy was 95.2% (table 3-7).

Table 3-7: comparison of LSM score with histopathology

<table>
<thead>
<tr>
<th>Cirrhosis (F4 vs F0-3)</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>F4</td>
<td>12(100%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>F0-F3</td>
<td>3(6%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15(24.2%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0(0%)</td>
<td></td>
</tr>
<tr>
<td>47 (94%)</td>
<td>47 (75.8%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50(100%)</td>
<td></td>
</tr>
</tbody>
</table>

Out of 62 patients enrolled in this study twelve patients were categorized by APRI score as F4 with cirrhosis, ten of them were positive in histopathology as F4 and two were negative. While 50 patients were categorized as F0-3 with no cirrhosis, 48 patients were positive in histopathological examination as F0-3, and 2 patients were false negative proved by histopathology as F4 with cirrhosis, so the APRI score Sensitivity was 83.3%, Specificity was 96%, PPV was 93.5, NPP was 96% and the Accuracy was 93.5% (table 3-8).

Table 3-8: comparison of APRI score with histopathology

<table>
<thead>
<tr>
<th>Cirrhosis (F4 vs F0-3)</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>F4</td>
<td>10 (83.3%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>F0-F3</td>
<td>2(4%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>12 (19.4%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>48 (96%)</td>
<td>50 (80.6%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

Out of 62 patients enrolled in this study 12 patients were categorized by LSM+APRI score as F4 with cirrhosis, 12 of them were positive in histopathology as F4 and no patients were negative. While 50 patients were categorized as F0-3 with no cirrhosis, 46 patients were positive in histopathological examination as F0-3, and 4 patients were false negative proved by histopathology as F4 with cirrhosis, so the LSM+APRI score the Sensitivity is 100% and the specificity is 92%, the PPV is 75% and the NPP is 100% finally the Accuracy is 93.5% as in (Table 3-9).
Table 3-9: comparison LSM + APRI score in F4 vs F0-F3 with histopathology

<table>
<thead>
<tr>
<th></th>
<th>Cirrhosis (F4 vs F0-3)</th>
<th>Total</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F4</td>
<td>F0-F3</td>
<td></td>
</tr>
<tr>
<td>LSM+APRI: Cirrhosis</td>
<td>12 (100%)</td>
<td>4 (8%)</td>
<td>16 (25.8%)</td>
</tr>
<tr>
<td>LSM+APRI: No</td>
<td>0 (0%)</td>
<td>46 (92%)</td>
<td>46 (74.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>12 (100%)</td>
<td>50 (100%)</td>
<td>62 (100%)</td>
</tr>
</tbody>
</table>

4.1 DISCUSSION.

Liver biopsy requires multiple lines of sampling, preservations, and interpretations. Nowadays, liver biopsy is certainly not the ideal procedure for assessment of liver fibrosis (89), (90), (91). Transient Elastography which is the first generation of elastography considered the gold standard elastography in assessing liver fibrosis. Point SWE is a recently developed method that is part of the second generation of ultrasound elastography methods. These methods differ from the TE in several aspects, including the generation of shear waves within the organ by a focused ultrasound beam and the capability of focusing the beam at different locations within the organ under ultrasound image guidance. These properties should improve the feasibility of stiffness measurements in obese patients and patients with ascites; they may also improve the accuracy of pSWE relative to TE. In addition to that the point SWE which is built in Ultrasound machine has others advantages over TE, that it can allow the evaluation of other parameters that are complementary to stiffness, including liver size, parenchymal echogenicity, portal vein diameter and blood velocity as well as splenic assessment (92), (93). A study done by Gerber et al., 2015 for evaluation of three different elastography procedures in assessment of liver fibrosis, included 132 patients with chronic hepatopathies, in which liver stiffness was evaluated using transient elastography, acoustic radiation force impulse imaging and 2-D SWE. The reference methods were liver biopsy for the assessment of liver fibrosis (n = 101) and magnetic resonance imaging/computed tomography for the diagnosis of liver cirrhosis (n = 31). No significant difference in diagnostic accuracy, assessed as the area under the receiver operating characteristic curve (AUROC), was found between the three elastography methods (2-D SWE, transient elastography, acoustic radiation force impulse imaging) for the diagnosis of significant and advanced fibrosis and liver cirrhosis in the "per protocol" (AUROCs for fibrosis stages ≥2: 0.90, 0.95 and 0.91; for fibrosis stage [F] ≥3: 0.93, 0.95 and 0.94; for F = 4: 0.92, 0.96 and 0.92) and "intention to diagnose" cohort (AUROCs for F ≥2: 0.87, 0.92 and 0.91; for F ≥3: 0.91, 0.93 and 0.94; for F = 4: 0.88, 0.90 and 0.89). Therefore, 2-D SWE, ARFI imaging and transient elastography seem to be comparably good methods for non-invasive assessment of liver fibrosis (94). Also Rizzo et al., 2011 found that ARFI was more accurate than TE for the staging of both significant and severe liver fibrosis (95). In our study which included 62 patients with chronic hepatic disease, the maximum number 50% had no previous medical history. The most prevalent viral infection was hepatitis B that was noted in 29% of the patients. This was followed by hepatitis C 11.3% and 3.2% had combined B and C viruses, this finding is comparable with Joyce et al in 2017 that represent the higher percent (14.1%) (96). No patient was recorded with human immunodeficiency virus in our study because it’s under diagnosis in our country. In this study the validity of gray scale ultrasonography is poor in assessing chronic liver disease, 48 patients out of 62 (77.42%) had normal parenchymal texture and 55 patient out of 62 (88.7%) with regular hepatic surface, this indicates that gray scale ultrasonography is insufficient imaging modality for proper assessment of the liver diseases, but in cases of liver cirrhosis, the sensitivity of gray scale is higher, usually the liver of small size, with coarse parenchymal texture and...
irregular surface in general the sensitivity and specificity of USG for cirrhosis is 91.1% and 93.1% respectively with 92.3% accuracy (Simonovský in 1999)(97). Regarding pSWE the mean value of LSM of the studied population was 12.5± 2.07 (Table 3.2). In comparison of F4 vs F0-3 LSM, AUROC was 0.986 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.962 while the upper bound was 1.0. If we take cut off value for LSM 13.9 this will give 100% sensitivity and 96% specificity. This finding was comparable with Giovanna et al.,2014 and Gerber et al.,2015. (98), (94). Our study showed that in comparison of F3-4 vs F0-2 LSM, the AUROC was 0.99 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.974 while the upper bound was 1.0. For the APRI score the AUROC was 0.948 with significant difference (P=0.0001) and the 95% confidence interval showed lower bound 0.90 and the upper bound was 0.99. If we considered a cut off value for LSM 7.6 this will give 95.8% sensitivity and 92.7% specificity. While a cut off value 1.15 for APRI score gave 91.7% sensitivity and 82.9% specificity (table 3-5), (Fig 3-6). To our best knowledge there was no research for comparism. In the current study comparing of F2-4 vs F0-1 LSM, the area under the curve was 0.98 with significant difference (P=0.0001) and the 95% confidence interval showed lower bound 0.956 while the upper bound was 1.0. For the APRI score the area under the curve was 0.931 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.87 and the upper bound was 0.988. A cut off value for LSM 6.8 gives 93.9% sensitivity and 90.6% specificity. And cut off value 0.75 for the APRI score gives 90.9% sensitivity and 75% specificity (table 3-6), (Fig.3-7). Our finding regarding area under the curve was 0.98, this was consistent with (Bavuet al.,2011)(67)(0.95) as well as with Ferraioliet al., 2012(99) (0.92) and higher than Anthony et al., 2015(100) (0.77). The mean value of APRI score for studied population was 1. 2 ± 0.8, out of 62 patients enrolled in this study twelve patients were categorized by APRI score as F4 with cirrhosis, ten of them were positive in histopathology as F4 and two were negative. while 50 patients were categorized as F0-3 with no cirrhosis, 48 patients were positive in histopathological examination as F0-3, and 2 patients were false negative proved by histopathology as F4 with cirrhosis, the AUROC was 0.959 with significant difference (P=0.0001) and the 95% confidence interval shows lower bound 0.913 and the upper bound was 1.0. So the APRI score Sensitivity was 83.3%, Specificity was 96%, PPV was 93.5, NPP was 96% and the Accuracy was 93.5% (tables 3-4 and 3-7), a cut off value of 1.35 for APRI score gives 91.7% sensitivity and 84.9% specificity. This finding is higher than the results of Prechchaisuratet al., 2012(101).Where the accuracy of APRI score was 72.88% with high sensitivity (90.48%) and high negative predictive value (92.31%). Many meta-analysis studies showed significant heterogeneity across the studies included. A systematic review and meta-analysis published in 2015 including 16 articles Xiao et al., 2015 (102). reported that APRI thresholds of 0.5, 1.0, and 1.5 yielded sensitivity and specificity values of 70% and 60%, 50% and 83%, and 36.9% and 92.5% for significant fibrosis, advanced fibrosis, and cirrhosis, respectively. This heterogeneity may be related to a fact that the AST could be elevated due to other factors rather than CLD, and different etiology of CLD. APRI score is considered to be one of the simplest and least expensive alternatives methods for assessing liver fibrosis have a number of advantages over histology including low cost, noninvasive and the absence of contra-indications such as thrombocytopenia or coagulopathy.

4.2 Limitations and problems
The number of ultrasound guided liver biopsies for the assessment of liver fibrosis has continued to reduce because of the increasing use of elastography which is noninvasive and without the side effects associated with liver biopsy. This diagnostic trend is reinforced by the continued
validation of elastography. Therefore, during this study, the recruitment rate was low. The ultrasound and elastography where all performed at the same site. Biopsy results were analyzed by more than one pathologists; this may have potentially led to variable histological inter-observer variability. There are limitations associated with elastography, including the confounding effects of inflammatory activity, and to a lesser extent, steatosis on liver stiffness evaluation (Belandet al in 2014). There is also reduced accuracy observed in lower fibrosis stages (F0-F2). A typical liver biopsy covers 1/10000\textsuperscript{th} of the liver while elastography covers a larger area. Matching the two sites covered by the two exams may not have been 100%. The information sort in the data collection form to analyze the secondary objectives was sensitive in nature including queries about alcohol use and HIV status. This precluded complete disclosure from participants and led to inadequate data on related parameters. This led to a reduction in the power of inferences regarding the role of alcohol and HIV.

**Conclusions**

1. Point SWE is a useful tool to screen for liver fibrosis in the general population during a conventional ultrasound examination, especially when laboratory tests and ultrasound examination are negative despite the potential underlying fibrosis.
2. Gray scale ultrasonography alone is insufficient imaging modality for full assessment of chronic liver disease.
3. A simple index like APRI, consisting of 2 readily available laboratory results (AST level and platelet count), can predict cirrhosis with high degree of accuracy. Besides being non-invasive, it can be determined at the bedside. It can also be of use in areas where facilities for liver biopsy and advanced imaging techniques are not available.

**Recommendations**

1. Epidemiological studies are needed to fully investigate the performance and utility of SWE in this setting.
2. We recommend a liver fibroscan should be done routinely in suspected cases of CLD.

Further prospective studies are needed to validate the APRI in a larger number of patients

**References**


