



TO ASSESS AND COMPARE LIVER ULTRASONOGRAPHIC ELASTOGRAPHY WITH OTHER SIMPLE NON INVASIVE SCREENING TOOLS IN CHRONIC LIVER DISEASE

Gastroenterology

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ABSTRACT

BACKGROUND: The prevalence of chronic liver disease is rising day by day; the need to stage the liver disease and fibrosis is accurately of paramount importance to guide therapy and know prognosis. Liver ultrasonographic elastography is an excellent tool for assessing fibrosis in patients with chronic liver disease. **AIMS AND OBJECTIVES:** To assess the liver stiffness with liver ultrasonographic elastography in different chronic liver diseases and compare it with APRI score. **STUDY DESIGN:** Cross-sectional study. **MATERIALS AND METHODS:** 100 patients attending to medicine outpatient department and patients who were admitted in medical wards of age more than 18 years with a detailed history suggestive of chronic liver disease and ultrasound abdomen showing altered echotexture of the liver between September 2018 to August 2019 were taken into our study. Fibroscan and other necessary investigations were done. **STATISTICAL ANALYSIS:** Student's t test, Chi-square test and Correlation were used to calculate the difference in the demographic and APRI and Fibro scan scores. ANOVA test was applied to determine the association of liver stiffness measurement, APRI and Fibro scan scoring system. P value <0.05 was taken as statistically significant. **RESULTS:** Out of 100 patients of CLD, Fibro scan suggested cirrhosis (F4) in 90 patients (90%) and APRI score (>1.5) suggested cirrhosis in 78% which was statistically significant with p value of 0.002. **CONCLUSIONS:** Fibroscan is a better investigation as compared to APRI score in detecting cirrhosis but not available at all places and also costly compared to APRI score.

KEYWORDS

Fibroscan, APRI Score, Cirrhosis Of Liver

INTRODUCTION

The prevalence of chronic liver disease is rising everyday and the need to stage the liver disease and fibrosis accurately is of paramount importance as it helps to guide therapy and inform prognosis. Liver biopsy is the gold standard associated with significant morbidity and mortality. The application of simple non-invasive tests to assess fibrosis could provide a safe way of identifying patients is the greatest need for intervention and monitoring response to therapy.

Liver ultrasonographic elastography is an excellent tool for assessing fibrosis in patients with chronic liver disease. It is easy to perform and correlates well with biopsy findings. There are many non-invasive screening scores for assessing fibrosis like aspartate-aminotransferase/platelet ratio index [APRI] score, AST/Alanine-aminotransferase [AAR], fib 4, etc which are widely available and cheaper than Elastography. Hence there is a need for comparing liver ultrasonographic elastography with other simple non-invasive techniques.

Liver stiffness (LS):

According to the theory of elasticity, Stiffness is defined as the modulus of elasticity. The liver, like any other soft tissue, stiffness depends on many factors.

- The first and foremost factor is extra cellular matrix of the organ. The extra cellular matrix can transfer external forces into the liver. It is the foundation for elastography.
- The second factor is the forces applied to the organ. The more pressure applied to the liver at its boundaries, the stiffer it gets.
- The third factor is an internal pressure inside the organ – if blood or another liquid is coming in and out, then the stiffness will depend on the resistance that the organ applies to the flow.
- The fourth and essential factor is the viscous effect which influences the time constant over which stiffness is applied. This effect is related to its frequency, i.e., stiffness depends on wavelength. While the liver is soft at the shallow rate (on the order of several hertz) which corresponds to manual palpation time-constant, it tends to be much harder at high frequencies (over several tens of kilohertz.)

Evolution of FibroScan:

The Fibro Scan (FS) (Echosens, Paris, France) device is the first elastography technique developed quantitatively and noninvasively to assess soft biological tissue stiffness *in vivo*. The Echosens adventure started after the thesis done by **Laurent Sandrin** under the supervision

of **Pr. Mathias Fink**.

He, together with an electronic engineer, called Jean-Michel Hasquenoph developed this technique and named it as Vibration Controlled Transient Elastography (VCTE). Echosens convened in June 2001 to convert this laboratory technique into a product.

How is the test performed?

With the patient lying in the supine position, an ultrasound-like a probe is placed on the skin over the liver area, typically in the right mid-axillary line. The patient feels a gentle 'flick' each time the probe generates a vibration wave. Usually, the test takes around 10 minutes to perform and causes no discomfort. In general, patients should have fasted for at least 2 hours before the procedure. Fibro Scan results range from 2.5 kPa to 75 kPa. Between 90–95% of healthy people with out liver disease will have a liver stiffness measurement <7.0 kPa (median is 5.3kPa).

SCORING SYSTEM IN FIBROSCAN

Healthcare provider will use Fibro Scan, fibrosis result and medical history to determine fibrosis score.

- F0 / F1: No liver scarring or mild liver scarring
- F2: Moderate liver scarring
- F3: Severe liver scarring
- F4: Advanced liver scarring (cirrhosis)

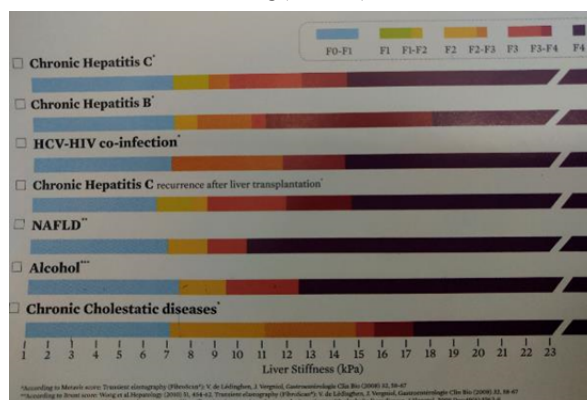


Figure No.1: Liver stiffness

The table below shows different chronic liver diseases, ranges of fibrosis results, and the matching fibrosis score. The varieties of fibrosis results in the table are estimates and actual fibrosis score may not match the fibrosis score in the table if one has more than one disease.

Table No. 1

Disease	fibrosis stage and approximate cut off values(Kpa)			
	F0-F1	F2	F3	F4
Hepatitis B	< 7.5	7.5 to 10.5	10.5 to 18	>18
Hepatitis C	< 7	7 to 12	12 to 14	>14
HIV/HCV CO-INFECTION	none	7 to 11	11 to 14	>14
CHOLESTATIC LIVER	2 to 7	7 to 9	9 to 17	>17
ALCOHOL	<7.5	7.5 to 9.5	9.5 to 12.5	>12.5

Liver biopsy is a gold standard in assessing liver fibrosis, but it is an invasive procedure and has complications. Hence, non-invasive methods like liver ultrasonic elastography and APRI score are used to assess fibrosis.

APRI SCORE :

Wai et al.²⁴ developed AST/platelet ratio (APRI) score in 2003. The upper reference limit for AST is taken as 40IU/L. APRI score greater than 1.0 has a sensitivity of 76% and specificity of 72% for predicting significant fibrosis. APRI score greater than 0.7 has a sensitivity of 77% and specificity of 72% for predicting significant fibrosis.

AST TO PLATELET RATIO INDEX (APRI)

Patient's AST/ULN AST(40)×100

Platelet count (10⁹/L)

• Interpretation:

<0.5=rules out significant fibrosis (F0-F1)

0.5 to 1.5=rules in significant fibrosis (F2-F3)

>1.5=cirrhosis (F4)

MATERIALS AND METHODS

100 patients attending to medicine outpatient department and patients who are admitted in medical wards of Sri Venkateshwara Ramnarain Ruia Government General Hospital, Tirupati between september 2018 to august 2019 with features of chronic liver disease on USG abdomen were examined with history and physical examination. Relevant investigations were done.

The detailed history of patients was taken and worked up for the etiology of chronic liver disease and patients are subjected to liver ultrasonographic elastography (fibro scan) in a fasting state, and results are tabulated between fibro scan scoring system and APRI scorings. Patients with mixed infections (hepatitis B + hepatitis C, HIV+ HBV, HIV+HCV,etc.), Acute on chronic liver disease patients and pregnant women were excluded from the study.

Statistics analysis

Student's *t* test, Chi-square test and Correlation were used to calculate the difference in the demographic and APRI and Fibro scan scores. ANOVA test was applied to determine the association of liver stiffness measurement, APRI and Fibro scan scoring system. P value <0.05 was taken as statistically significant.

RESULTS AND DISCUSSION

In our study, the most common age group affected is of 41-50 years, which constitutes 31% followed by 31-40 years, which constitutes 24%. The oldest patient in this study is 73 years, and youngest being 25 years. The mean age is 44.03± 11.191 years. Males(81%) are affected more than females(19%).

In our study, majority of the study population are ethanol related CLD(53%). Patients with HBV related CLD(25%) and HCV related CLD(22%) are almost equally distributed.

In the present study, fibro scan suggestive of cirrhosis (f4) was noted in 90 cases (90%). Among them ethanol related CLD, HBV related CLD, HCV related CLD constituted 49(49%), 22(22%) and 19(19%)

respectively.

Fibro scan not suggestive of cirrhosis (f0-f3) was noted in 10(10%) cases, among them ethanol related CLD, HBV related CLD, HCV related CLD constituted 4(4%), 3 (3%) and 3(3%) respectively.

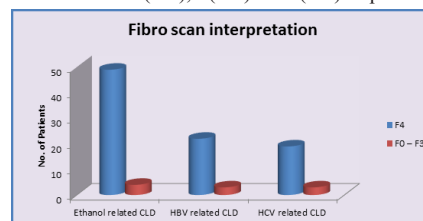


Figure No 2 : Fibro scan interpretation in study population



Figure no.3 : Example of a Fibro scan reports of patients

In our study, APRI score suggestive of cirrhosis (>1.5) was noted in 78 cases (78%). Among them ethanol related CLD, HBV related CLD, HCV related CLD constituted 40(40%), 20(20%) and 18(18%) respectively.

APRI score not suggestive of cirrhosis (≤1.5) was noted in 22 (22%) cases, among them ethanol related CLD, HBV related CLD, HCV related CLD constituted 13 (13%), 5 (5%) and 4 (4%) respectively.

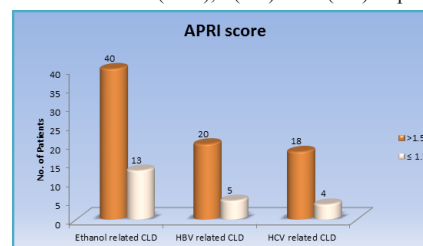


Figure No 4 : APRI score in study population

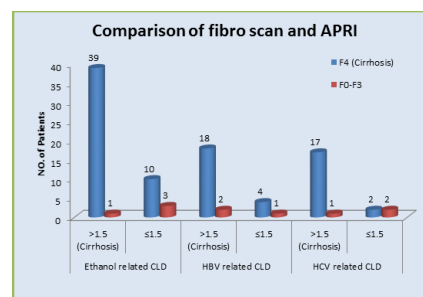


Figure No 5 : Comparison of Fibro scan with APRI score in CLD patients of various etiologies

Table No 2 : Comparison of fibro scan with APRI score in various studies

Fibro Scan		APRI SCORE
Present study	Pearson correlation(r value)	0.257**
	Significance(p-value)	0.002
Deping ding et al ⁶⁸	Pearson correlation (r)	0.313
	Significance (p)	0.001
Shishirendu Parihar et al ⁷¹	Pearson correlation (r)	0.519
	Significance (p)	0.026

N = 100. Correlation is significant at the 0.01 Level * P < 0.05 **P< 0.01

Deping Ding et al⁶⁸ conducted Pearson correlation analysis between LS and APRI and the related coefficient was 0.313.

SUMMARY & CONCLUSIONS

- In our study, fibro scan is suggestive of cirrhosis in 90% of patients who are diagnosed to have CLD by ultrasound.
- Fibro scan can be used to assess liver stiffness for evaluation of disease progression in patients with CLD.
- APRI score showed that there is a significant concordance with fibro scan in detecting cirrhosis.
- Hence APRI score can be used in limited resource settings where fibro scan is not available and in patients who are not affordable for fibro scan

ABBREVIATIONS

AST	:	Aspartate aminotransferase
APRI	:	AST to platelet ratio index
AAR	:	AST/ALT ratio
ALT	:	Alanine aminotransferase
CLD	:	Chronic liver disease
HBV	:	Hepatitis b virus
HCV	:	Hepatitis c virus
Kpa	:	Kilopascals

REFERENCES

1. Anthony PP, Ishak KG, Nayak NC, Poulsen HE, Scheuer PJ, Sobin LH. The morphology of cirrhosis. Recommendations on the definition, nomenclature, and classification by a working group sponsored by the World Health Organization J Clin Pathol 1978; 31: 395-414.
2. Horbin WP et al. Diagnosis of cirrhosis based on regional changes in hepatic morphology. Radiology, 1980; 135: 273.
3. Lee UE, Friedman SL. Mechanisms of hepatic fibrogenesis. Best Pract Res Clin Gastroenterol 2011; 25: 195-206.
4. Crespo G, Fernandez-Varo G, Marino Z, et al. ARFI FibroScan, ELF, and their combinations in the assessment of liver fibrosis: A prospective study. J Hepatol 2012; 57: 281-7.
5. Robic MA, Procopet B, Metivier S, et al. Liver stiffness accurately predicts portal hypertension related complications in patients with chronic liver disease: A prospective study. J Hepatol 2011; 55: 1017-24.
6. Castera L, Forns X, Alberti A. Non-invasive evaluation of liver fibrosis using transient elastography. J Hepatol 2008; 48: 835-47.
7. Ajay Pratap Singh, Ravi Misra, Assessment of Liver Fibrosis by Transient Elastography and APRI (AST to Platelet Ratio) in patients with Chronic Liver Disease. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 17, Issue 01 Ver. III January, (2018), PP 79-85.
8. N. Frulio, H. Trillaud ultrasound elastography in liver, diagnostic and interventional imaging, 2013, 94, p515-534.
9. Nahon P et al. Assessment of liver fibrosis using transient elastography in patients with alcoholic liver disease. J Hepatol. 2008 Dec; 49(6): 1062-8 (PRINCI ET AL).
10. Stephanie Wong, Dep Huynh, Frank Zhang, Nam Q Nguyen, Use of aspartate aminotransferase to platelet ratio to reduce the need for Fibro Scan in the evaluation of liver Fibrosis, World J Hepatol 2017 June 18; 9(17): 791-796.
11. Deping Ding, Hongbing Li, Ping Liu, Lingli Chen, Jian Kang, Yinhua Zhang et al., Fibro Scan, aspartate aminotransferase and alanine aminotransferase ratio (AAR), aspartate aminotransferase to platelet ratio index (APRI), fibrosis index based on the 4 factor (FIB-4), and their combinations in the assessment of liver fibrosis in patients with hepatitis B, nt J Clin Exp Med 2015; 8(11): 20876-20882.