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Original Research Article

Liver fibrosis assessment: a correlation of fibro scan values with gray scale assessment of portal vein

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ABSTRACT

Background: FibroScan is an expensive modality with excellent accuracy for diagnosis of cirrhosis by measuring liver stiffness. In less developed countries it is not a financially viable method for fibrosis measurement. The aim of this study is to compare and correlate FibroScan values with gray scale sonographic assessment of portal vein calibre diameter which can be done using a basic ultrasonography machine.
Methods: Prospective review of 124 patients with chronic liver disease done between Dec 2015 to May 2016 with the objective of correlating FibroScan values with gray scale assessment of portal vein.
Results: In our study 50 patients had liver stiffness scores of > or = 7.5 kPa and above. A total of 45 patients had a respiratory phase variation of portal vein calibre of < 20%. Out of these, 37 patients had a liver stiffness score of 7.5 kPa or above. These 37 patients were correctly classified by portal vein calibre variability as having moderate to severe fibrosis. The results of this study revealed a significant correlation (Pearson coefficient, r = -0.617, p= 0.01) between calibre variation of the portal vein and FibroScan scores. We also noted that in presence of mild fibrosis as predicted by lower FibroScan scores, PV calibre variation is not a reliable indicator of mild fibrosis.
Conclusions: We propose that, in less developed countries, gray scale assessment of portal vein diameter using any low cost ultrasound machine can be used as an optimal method for predicting moderate to severe liver fibrosis.

Keywords: FibroScan, Liver fibrosis, Portal vein calibre variation, Transient elastography

INTRODUCTION

Chronic liver disease is an important public health related problem. Hepatic injury in any form has the same pattern of progression i.e. inflammation followed by necrosis, fibrosis¸ regenerative nodule formation leading to cirrhosis and later carcinoma. Progressive fibrosis of liver with subsequent development of cirrhosis is seen in almost all types of chronic liver diseases. A number of complications are associated with cirrhosis. Prognosis and management depends on the severity of fibrosis. Portal hypertension is main characteristic of liver cirrhosis. The degree of liver stiffness has been established as a strong indicator of advanced fibrosis or cirrhosis. Various non-invasive tests are being developed for predicting fibrosis in chronic liver disease. Out of these, a promising method is transient elastography which measures liver stiffness.[1] Liver stiffness has excellent accuracy for diagnosis of cirrhosis. However, it is an expensive modality. So, there is a necessity to look for low cost alternative methods with a similar sensitivity and specificity.

Portal vein calibre variation is an established sonographic sign of portal hypertension. It is a cost effective non-invasive method that can be utilised in a peripheral set up. However, its value as an accurate predictor of fibrosis still needs to be compared with a gold standard.

Aim of this study was to study correlation between transient elastography and portal vein diameter variation.

METHODS

Patients

The study was carried out in a north Indian tertiary care hospital from Dec 2015 to May 2016.

A total of 124 patients with chronic liver diseases from gastrointestinal outpatient department (GI OPD) were prospectively included. Standard diagnostic criteria were used to diagnose chronic liver disease. Serological tests were used for diagnosing Hepatitis C or Hepatitis B. Patients consuming at least 40 g of alcohol daily for five years or more were diagnosed with alcoholic liver disease. Consent was given by all patients.

The following parameters were taken into consideration for liver stiffness measurement- weight, height and ascites. Laboratory tests included Liver function test, platelet count, prothrombin time and albumin. Upper gastrointestinal endoscopy was done in all patients which revealed no abnormality.

Measurement of liver stiffness

Patients were made to lie in the dorsal decubitus position with the right arm avoiding the body. The examinations were completed utilizing an Abott FibroScan VCTE (Vibration controlled transient elastography). Estimations were performed through intercostal spaces in the right upper quadrant at the level of the right lobe of liver. The transducer probe was placed on the skin after applying gel. The examiner selected a liver segment of no less than 6 cm thick free of any blocking structures pressed the probe switch to start an acquisition. The depth under the skin at which the test was performed was around 20 mm and 50 mm. The outcomes are communicated in kilopascal (kPa) (Figure 1). Estimations which were wrong were erased by intrinsic dismissal programming. Up to 10 estimations were performed on every patient. Success rate was computed by the quantity of effective estimations over the aggregate number of acquisitions. Liver stiffness estimations with no less than five fruitful estimations or a win rate of no less than 25% were viewed as dependable.

Measurement of portal vein caliber variation

The patients were kept fasting for at least 8 hrs. The scans were carried out using Logiq P5 ultrasound machine with a 5.0 MHz transducer (Figure 1).

Measurements were carried out in the supine position. The scans were performed during inspiration and expiration. The portal vein was imaged along its long axis, and the antero-posterior diameter measured at its widest point at porta hepatis.

Inclusion criteria

A total of 124 patients with chronic liver disease from GI OPD were examined.

Exclusion criteria

Patients having ascites and morbid obesity were excluded. Patients with established cirrhosis on USG were excluded.

RESULTS

In this study, among 124 patients, 50 had liver stiffness scores of > or = 7.5 kPa and above. A total of 45 patients had a respiratory phase variation of portal vein calibre of < 20%. Out of these, 37 patients had a liver stiffness score of 7.5 kPa or above. Compared with liver stiffness, these 37 patients were correctly classified by portal vein calibre variability as having moderate to severe fibrosis, whereas 13 patients differed and showed phase variability of > 20%. The results of this study showed significant correlation (Pearson coefficient, r = -0.617, p= 0.01) between calibre variation of the portal vein during respiration and FibroScan scores using the IBM SPSS software. We also noted that in presence of mild fibrosis as predicted by lower FibroScan scores, portal vein calibre variation did not turn out to be a reliable indicator of the same. Out of the 74 patients with FibroScan scores of < 7.5 kPa, only 8 patients showed a portal vein calibre phase variation of < 20%.

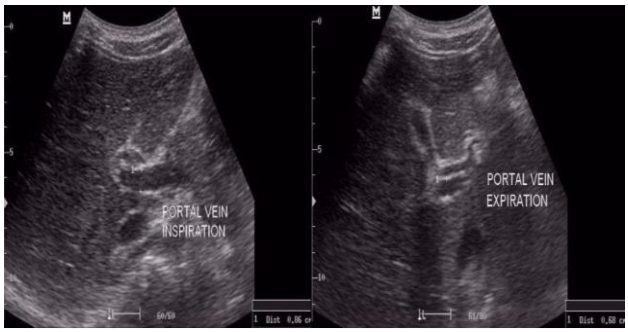

Figure 1: Changes in portal vein diameter on inspiration and expiration.

DISCUSSION

The value of transient elastography (TE) has been explored in a number of studies. The degree of liver stiffness has been established as a strong indicator of advanced fibrosis or cirrhosis.[2] Although liver biopsy still remains the gold standard for evaluating liver fibrosis; it is fraught with several disadvantages, such as invasiveness, painful procedure, intra- and inter-observer variations.[3,4] Therefore, in practice, liver biopsy is not always an acceptable method for monitoring. As a result of these limitations, focus has been directed towards development of better methods for assessment of liver

fibrosis, preferably non- invasive. Various non-invasive tests are being developed for predicting fibrosis in chronic liver disease. Out of these, a promising method is transient elastography which measures liver stiffness. Lupsor M et al state that "Liver stiffness has high accuracy for diagnosis of cirrhosis with AUROC of 0.9-0.99 for cut-off values ranging from 9 to 26.6 kPa. The best appeared to be 13.01 kPa".[2] As stated by Pinzani M et al -"The values are reproducible, operator-independent and correlate well with the degree of fibrosis".[5] Therefore, it has a potential to be, if not the gold standard, but definitely, the best non-invasive reference for evaluating liver fibrosis. Liver stiffness is not just a tool for measuring liver fibrosis. It also helps in assessing the clinical course of CLD patients. It can assess the complications as well as useful for long term risk classification and stratification.

Shear wave elastography can evaluate the differences in the elastic properties of various soft tissues by measuring the differential behaviour of tissues when a mechanical force is applied. It works on the principle of generation of shear waves when underlying tissues are displaced by the force of an ultrasound beam which acts as the mechanical force. These shear waves travel in a direction perpendicular to that of the force applied. They travel at a slow rate (between 1 and 10 m/s) and get attenuated by the intervening obstructions in their course. The propagation velocity of the shear waves correlates well with the elasticity of tissue and is directly proportional to the stiffness of the liver parenchyma.

FibroScan is a recently developed instrument used for assessing transient elasticity. It expresses stiffness of the liver in kilopascals (kPa). A number of studies have compared FibroScan values to fibrosis estimated by liver biopsies. These studies have revealed a direct relationship of liver stiffness and fibrosis staging. In a study conducted by Sandrin et al, "the median hepatic elasticity was 4.2 kPa for F0 fibrosis score, 4.5-6.25 kPa for F1 fibrosis score, 5.5-7.8 kPa for F2 fibrosis score, 8.0-13.7 kPa for F3 fibrosis score, and 21–34 kPa for a F4 fibrosis score".[3] Various other studies have reported similar results for a range of liver diseases. According to Foucher J et al," cut off values of liver stiffness were 7.2 kPa and 12.5 kPa for moderate and severe cirrhosis.[6] A recommended threshold of 17.6 kPa and 14.6 kPa for the diagnosis of cirrhosis, with sensitivities of 77% and 79%, specificities of 97% and 95%, and positive predictive values of 91% and 74%, respectively was offered by two studies." - A recent meta-analysis of 9 published studies showed "87% for sensitivity and 91% for specificity for stage 4 fibrosis (cirrhosis).[7] In patients with stage 2-4 fibrosis the estimated sensitivity is 70% and specificity is 84%." Therefore, with such high sensitivity and specificity, FibroScan can easily replace biopsy as a non-invasive tool for accurately detecting fibrosis and can be helpful for screening of cirrhosis. Biopsy can be avoided in a large number of patients, if FibroScan is used as screening tool. In a peripheral set up, where there is a scarcity of resources performing liver biopsy or even the option of using FibroScan to accurately predict fibrosis may not be feasible. At the most, grey scale ultrasound machine may be the only available resource in such a set up. So, there is a necessity to look for low cost alternative methods with a similar sensitivity and specificity as that of liver biopsy or FibroScan.

The aim of this study is to demonstrate the relationship of the calibre variation of the portal vein during respiration using a grey scale B- mode ultrasound machine and a non-invasive gold standard like measurement of liver stiffness using FibroScan and hence, determine the effectiveness of portal vein calibre variation with respiration (an indicator of portal hypertension) as a screening tool for fibrosis.

A number of studies have been conducted to establish the correlation between portal hypertension and liver stiffness values.[8-11] Portal hypertension in these studies was assessed either by the presence of oesophageal varices seen endoscopically or by measuring hepatic venous pressure gradient. According to our knowledge, there are no available reports about the correlation of portal hypertension assessed by respiratory phase variation of portal vein diameter with any of the gold standards like liver biopsy or liver stiffness measurements. Previously, one study had only demonstrated a lack of normal calibre variation (an increase during inspiration and a decrease during expiration) in portal vein as an ultrasonographic sign of portal hypertension. An increase of less than 20% in the diameter of the portal vein with deep inspiration indicates portal hypertension with 81% sensitivity and 100% specificity.

The available studies were only capable of proving calibre variation of portal vein as a sensitive indicator of portal vein hypertension and the possibility of presence of fibrosis. Ours is a pilot study first of its kind that shows a definite correlation between respiratory phase variation of portal vein diameter and an established reference standard like liver stiffness which is a direct indicator of liver fibrosis. Thus, we attempt to prove its reliability as an accurate predictor of liver fibrosis.

Our study revealed significant correlation (Pearson coefficient, $r = -0.617$, $p = 0.01$) between calibre variation of the portal vein during respiration and FibroScan scores. Portal vein calibre variation is a reliable indicator of moderate to severe fibrosis. However, it is not a reliable indicator of mild fibrosis.

Study limitations: Our study is restricted by the limited size of our group of patients. In addition, the patients were known cases of chronic liver disease and thus not illustrative of the general population.

A further impediment of FibroScan itself is that its values are not accurate in all patients with liver cirrhosis.[12,13]

Patients with ascites and high grade fatty liver are not amenable to assessment by FibroScan.[14,15] While patients with BMI ≥35kg/m2 were kept out of the study as the thickness of their subcutaneous fat layer impacts the legitimacy of results.

CONCLUSION

Variation of calibre of portal vein with respiratory phases of < 20 % is a good indicator of moderate to severe fibrosis. Therefore, in a peripheral setting, respiratory phase variation measurement of portal vein diameter using any low cost grey scale ultrasound machine can be used as an optimal method for predicting liver fibrosis.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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