Doppler Ultrasound and Fibroscan Parameters Versus Liver Biopsy in Evaluation of Hepatic Fibrosis in Egyptian Patients with Chronic Hepatitis C

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Key words:
Fibroscan, Hepatitis C, Doppler

Background and study aim: Liver biopsy is the gold standard method to assess hepatic inflammation and fibrosis in chronic hepatitis C infection (HCV). The non-invasive assessment of liver fibrosis is the key target that has inspired many new methods because of the limitations of liver biopsy. The aim of the work was to improve the efficiency of non-invasive liver fibrosis assessment in Egyptian patients with chronic hepatitis C by comparing Doppler ultrasound (US) of hepatic blood flow and fibroscan with liver biopsy.

Patients and Method: In this retrospective analysis, 78 patients with HCV had already undergone liver biopsies as part of work panel prior to HCV treatment. Fibroscan examination, abdominal ultrasonography and Doppler ultrasound were done to the patients by experienced operators.

Results: There was a strong positive correlation between the degree of liver fibrosis by fibroscan and the degree of inflammation in the histopathological analysis. Receiver Operator Characteristic (ROC) curve analysis revealed that fibroscan failed to detect FII fibrosis. However, fibroscan was more accurate in detecting FIII fibrosis.The Doppler ultrasound parameter ROC curve analysis, the portal vein blood flow volume (PVBFV) was shown to be more accurate in detecting lower grades of fibrosis than higher.

Conclusion: For detection higher degrees of fibrosis, Fibroscan has a strong match with liver biopsy; however, Doppler US is more sensitive in detecting lower grades of fibrosis in patients infected with HCV .

INTRODUCTION

Egypt has the highest incidence of hepatitis C (HCV) infection worldwide with major public and economic health burden [1]. With persistent liver damage; fibrosis can progress to cirrhosis in up to 15% to 20% of cases within 20 years [2]. An estimation of fibrosis progression is critical for assessing the outcome of HCV infection. The gold standard for assessing the grade of liver fibrosis is liver biopsy, which provides diagnostic information not only on fibrosis but also on many other processes of liver damage, such as necrosis, inflammation, steatosis, copper or iron hepatic deposits [3].

Because of its complications, such as bleeding or pain, sampling error can occur in up to 25% of cases with biopsy perception inter- and intra-observer variability [4] and its limitation in distinguishing between stages F1 and F2 of fibrosis [5] and, in order to assess the severity of liver fibrosis, non-invasive methods have been developed [6]. The non-invasive tools available are either "biological" methods based on serum fibrosis biomarker levels or "physical" methods based on the measurement of liver stiffness using transient elastography [7].

Ultrasound-based elastography has led to a breakthrough in the assessment of fibrosis by different methods: one-dimensional ultrasound elastography-transient elastography (TE); or two-dimensional ultrasound (or B-mode) using conventional ultrasound imaging-acoustic radiation force (ARFI) imaging or point shear wave elastography (pSWE), real-time 2D shear wave elastography (2D-SWE) and real-time elastography (RTE) [8].

The first ultrasound-based elastography for the diagnosis and staging of liver fibrosis [9] is transient elastography (Fibroscan®, Echosens, Paris). By calculation of low- frequency elastic shear wave velocity distributed through the liver, TE uses a mono-dimensional ultrasound to estimate liver stiffness. TE can be accomplished in brief periods and has outstanding (typically less than 5 minutes) intra- and inter- observer variability [10].

Ultrasound is the screening tool for initial assessment of the liver. With the appearance of Doppler ultrasound carried non-invasive means to evaluate secondary changes of blood circulation to chronic liver disease. It could detect the decrease of the portal vein flow velocity and caliber increases, both indicative of portal hypertension [12]. Through the comparison of Doppler ultrasounds of hepatic blood flow and fibroscan with liver biopsy, we aimed to enhance the non-invasive assessment of liver fibrosis in Egyptian patients with chronic hepatitis C.

METHODS

This was a retrospective comparative observational analysis, with a purposive convenience nonrandomized sample. The informed consent form authorizing the collection of this data was signed by all patients. 250 medical records were reviewed and 78 patients were enrolled with chronic HCV genotype 4 infection. The inclusion criterion included chronic HCV- infected patients aged 18 years or older, male or female, who were assessed for treatment (pegylated interferon and ribavirin) under the national therapeutic regimen.

Exclusion criteria:

1- Any medical history of compensated or decompensated congestive heart failure to prevent influence of retrograde hepatic blood flow caused by cardiac reflux

2- History of decompensated liver disease

3- Post liver transplantation (to prevent anastomosis affecting blood flow measurement)

4- Pregnancy

5- Age less than 18 years

6- Hepatitis B virus co-infected patients

We used the free sample size calculator for cohort study at (http://www.openepi.com/SampleSize/SSCohort.htm) to calculate the sample size for this study. At test power of 0.8 and confidence interval of 95%, sample size was assumed to be 74 patients

Liver biopsy specimens were obtained under complete a septic procedures to retrieve 15mm core or at least 15 portal tracts.The specimen was processed and stained with hematoxline and eosine. Fibrosis was tagedona 0ñ 4scale:F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis and few septa; F3, numerous septa without cirrhosis; and F4, cirrhosis according to METAVIR scoring system [11].

Liver biopsies were taken from 78 HCV-infected Egyptian patients as a part of the work-up before HCV treatment. Fibroscan analysis, abdominal ultrasonography, and Doppler ultrasound were performed by a qualified operator who has no data of the patient's clinical history, biochemical examination, or histo pathological results.

All records of the patients are documented in the hospital inpatient and outpatient clinics in the Tropical Medicine Department of Tanta University Hospital, Tanta, Egypt.

All patients were exposed to

- History taking, complete clinical examination, laboratory tests including the full blood analysis, blood urea , serum creatinine the liver function tests (liver enzymes, albumin and bilirubin), prothrombin time, activity, and APRI score were calculated in each patient, and patients were then exposed to:

- Abdominal ultrasonography.

- Transient Elastography (Fibroscan): The hepatic stiffness measurements were conducted by skilled operators following the

manufacturer's recommendations, using the 502M fibroscan (echosens-France) probe. It was performed with the patient in supine posture and totally abducted by the right arm from the intercostal transthoracic window on the right liver lobe.

The interquartile range (IQR) was considered accurate with a score of less than 30 % and a success rate of not less than 70 %. The median value was known to be an indication of the elastic state of the liver. The median value was determined automatically by the software, and the results were expressed in Kilopascals (kPa). All measurements were done with the FibroScan (M) probe after a fasting period of 6 hours. The elastogram score obtained by the device is interpreted through special software to identify the corresponding fibrosis stage in the Metavir score.

- Doppler ultrasound was done by using Toshiba Nemio XG apparatus with a convex probe 3.5 MHz to assess:

a)   the diameter of the portal vein and the volume of the portal vein blood flow

b) the Hepatic venous resistance index (HVRI) for the right hepatic vein

c) The Hepatic artery resistance index (HARI)

d) The Hepatic artery pulsatility index (HAPI)

e) The Splenic artery resistance index (SARI)

The normal diameter of portal vein is highly variable but does not exceed 16mm in a resting state on quiet respiration [43]. Normal hepatic artery RI was reported by McNaughton and Abu-Yousef, to be 0.55–0.7 [44], while normal hepatic pulsatility index was reported by Schneider et al, to be 0.92±0.1 [45]. The normal value of splenic artery resistive index (SARI) was reported by Loanitescu to be 0.51 +/- 0.05 [46].

Ethical consideration

Institutional ethical committee approval was obtained before the start of the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a prior approval by the institution's human research committee.

Statistical analysis:

The data was analyzed using version 2 of Sigma Stat. Quantitative data are presented as mean and SD while qualitative data are expressed as number and percent. Non-normally distributed data are expressed as range (min-max) and median.

Difference among groups was performed using independent-sample student t-test between groups when normally distributed or ManneWhitney U test if not normally distributed.

The Receiver Operator Characteristic (ROC) curves were developed to assess the accuracy of the diagnosis prediction of fibrosis using version 13.0 of the Social Sciences Statistical Package (SPSS) (IBM Corp, Armonk, NY, USA). The areas of individual tests with 95% confidence intervals under ROC curves (AUCs) were calculated and compared. The coefficient of Correlation was measured by Spearman's correlation. The findings were found statistically significant when $p < 0.05$ for all used tests.

RESULTS

This retrospective research was conducted on 78 HCV patients with a mean age of 43.17 ± 10.77 years and 37 (47.4%) males. There was no statistical difference in (AST to Platelet Ratio Index) APRI score among patients categorized according to fibrosis degree in liver biopsy (P> 0.05).

Sixty patients had abnormal findings in ultrasound; 20 patients had bright liver, 12 patients had periportal fibrosis, and 28 had ultrasonic findings of liver cirrhosis as coarse echo pattern, irregular outlines, enlarged caudate lobe and shrunken liver in some patients. Regarding splenic examination 16 patients had splenomegaly. The kidney examination in all patients showed normal size and good differentiation between cortex and medulla except for one patient who had grade one nephropathy.

According to fibrosis and activity detected by liver biopsy:

- According to fibrosis degree according to METAVIR scoring system[11]: 57 patients with mild fibrosis (F1 and F2) and 21 patients with significant fibrosis (F3).

- According to activity degree: 35 patients with mild activity (A1) and 43 patients who showed moderate to severe activity (A2-A3)

In order to evaluate the fibroscan results (figure 1):

There was a statistically significant difference in fibroscan results with higher scores detected in higher fibrosis P<0.001 and more activity (A2 and A3) in liver biopsy P<0.001. The degree of fibrosis in liver biopsies was significantly correlated with liver texture in ultrasound (r=0.430, p=0, 00245) and fibroscan (r=0.51, p<0.001). Also, the activity degree showed a significant positive correlation in liver biopsy with fibrosis degree (r=0.49, p<0.001). The ROC curve analysis showed that fibroscan failed to detect FII fibrosis (AUC 0.243, 95% confidence interval (CI) 0.074-0.411). However, fibroscan was more accurate in detecting F3 fibrosis (AUC = 0.816, 95% CI 0.666-0.971) at cut off values ≥7.95 kPa fibroscan had 85.7 % sensitivity and 60.5 % specificity in detecting F3 fibrosis.

The analysis of Doppler ultrasonic parameters of the liver:

The normal diameter of portal vein is highly variable but does not exceed 16mm in a resting state on quiet respiration [43].

There was a statistically significant decrease in portal vein flow volume (P<0.001) in moderate fibrosis in comparison to mild fibrosis

also, Portal vein flow volume was decreased significantly in the patients when compared to the average documented values P <0.001, Also a significant negative correlation between fibrosis degree in liver biopsy and portal vein flow volume was found (r= - 0.55 , p <0.001). No statistical differences in splenic artery resistance index (SARI) , hepatic artery resistance index (HARI), and hepatic artery pulsatility index (HAPI) (P> 0.05) between the two groups, however, in our patients ,HARI , HAPI , and SARI were significantly higher compared to the average documented values (p=0.03,<0.001 and <0.001 respectively). There was no difference in results of HARI, HAPI, SARI, HVRI among patients with mild and moderate activity compared to patients with severe activity in the liver biopsy as shown in cases (figure 3-5).

As regards ROC curve of portal vein blood flow volume for the detection of fibrosis degree in liver biopsy; For F2, AUC was 0.645 (95% CI = 0.424-0.866). At a cut-off point ≤ 0.443 L/min, the portal vein blood flow volume had sensitivity of 76.9% and specificity of 60% in detecting F2 hepatic fibrosis in liver biopsy and For F3, it was not an accurate method (AUC = 0.201, 95% CI=0.61-0.340) figure 2.

Table (1): Comparison between patients activity in liver biopsy and fibroscan elasticity score

All patients (n=78)	Mild activity (A1) (n=35)	Moderate to severe activity (A2-A3) (n=43)	T	P
Range (KPa) Mean ±SD Median	3.4-10.2 5.94±1.98 5.57	3.8-38 11.93±8.18 8.3	-2.878	0.005*

Significant (P<0.05).

Table (2): Portal vein blood flow volume (PVBFV), hepatic artery resistance index (HARI), hepatic artery pulsatility index (HAPI) and splenic artery resistance index (SARI) among our patients in comparison with normally decoumented values

	Normal range	All patients	t- test	P value
PVBFV(l/min) Mean ±SD	0.864±0.188(13)	0.625±0.336	4.389	<0.001*
HARI (cm^3/s) Mean ±SD	0.65±0.1(14)	0.72±0.12	-3.169	<0.002*
HAPI (cm^3/s) Mean ±SD	0.92±0.1(15)	1.33±0.42	-6.715	<0.001*
SARI (cm^3/s) Mean ±SD	0.51±0.05(16)	0.664±0.12	-8.684	<0.001*

Significant (P<0.05).

Table (3): Comparison between patients with mild and moderate fibrosis in liver biopsy regarding fibroscan elasticity score and Doppler parameters

	Mild fibrosis (FI-FII) (n=57)	Moderate fibrosis (FIII) (n=21)	t	P
Fibroscan score Range(KPa) Mean ±SD Median	3.4-38 8.82±6.4 7.3	7-33.3 17.34±9.12 16.8	2.137	0.038*
PVD(mm) Range Mean ±SD Median	7.6-20 12.34±2.54 12.3	9.2-14.8 12.17± 2.12 12	0.161	0.868
PVBF (L/min) Range Mean±SD Median	0.102-1.478 0.675±0.33 0.64	0.051-0.63 0.33±0.199 0.284	2.674	0.01*
HARI (cm³/s) Range Mean ±SD Median	0.54-0.94 0.732±0.106 0.73	0.41-0.89 0.657±0.195 0.62	1.531	0.132
HAPI (cm³/s) Mean ±SD Range Median	1.343±0.412 0.53-2.09 1.33	1.263±0.539 0.59-2.15 1.145	0.452	0.653
SARI(cm³/s) Mean±SD Range Median	0.67±0.12 0.45-0.95 0.65	0.65±0.056 0.59-0.75 0.64	0.380	0.705

Significant (P<0.05)   PVD = Portal vein diameter and PVBFV= portal vein blood flow volume
Hepatic artery resistance index (HARI)   Hepatic artery pulsatility index (HAPI)
Splenic artery resistance index (SARI)

Table (4): Correlation between fibrosis degree in liver biopsy and biochemical tests, fibroscan, ultrasound, and Doppler parameters

	R	P
ALT	0.077	0.593
AST	0.029	0.842
Albumin	-0.267	0.061
Fibroscan	0.284	0.045*
liver texture by ultrasound	0.430	0.002*
PVD	0.038	0.792
PVBFV	-0.410	0.004*
HARI	-0.146	0.322
HAPI	-0.189	0.197
HVRI	-0.254	0.075
SARI	-0.0123	0.932

Significant (P<0.05)
ALT= alanine aminotransferase
AST= aspartate aminotransferase
PVD = Portal vein diameter and PVBFV= portal vein blood flow volume
Hepatic vein resistance index (HVRI) of right hepatic vein
Hepatic artery resistance index (HARI)
Hepatic artery pulsatility index (HAPI)
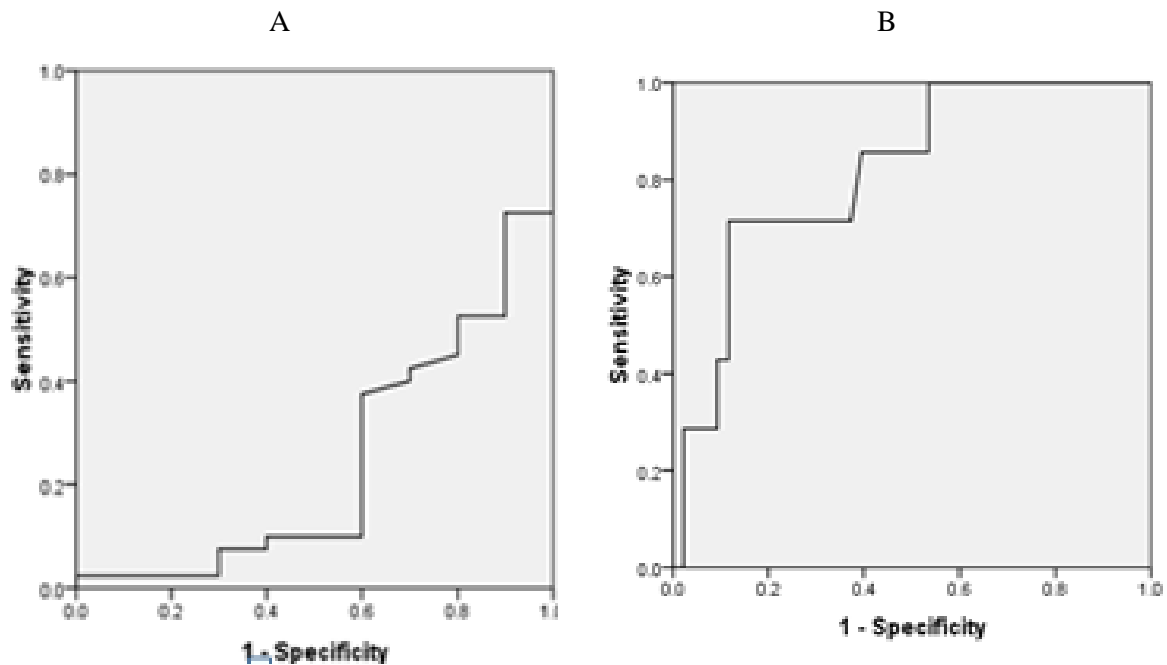Splenic artery resistance index (SARI)

A   B

Fig (1): The Receiver Operator Characteristic (ROC) curve of fibroscan to detect fibrosis degree in liver biopsy. (A) For F2, It was not accurate method (AUC= 0.243, 95% CI=0.074-0.411). (B) For F3, AUC was 0.82 (95% CI=0.66-0.97). At a cut-off point ⩾ 10.9 kPa, fibroscan had sensitivity of 71.4% and specificity of 83.7 % in detecting F3 hepatic fibrosis in liver biopsy.
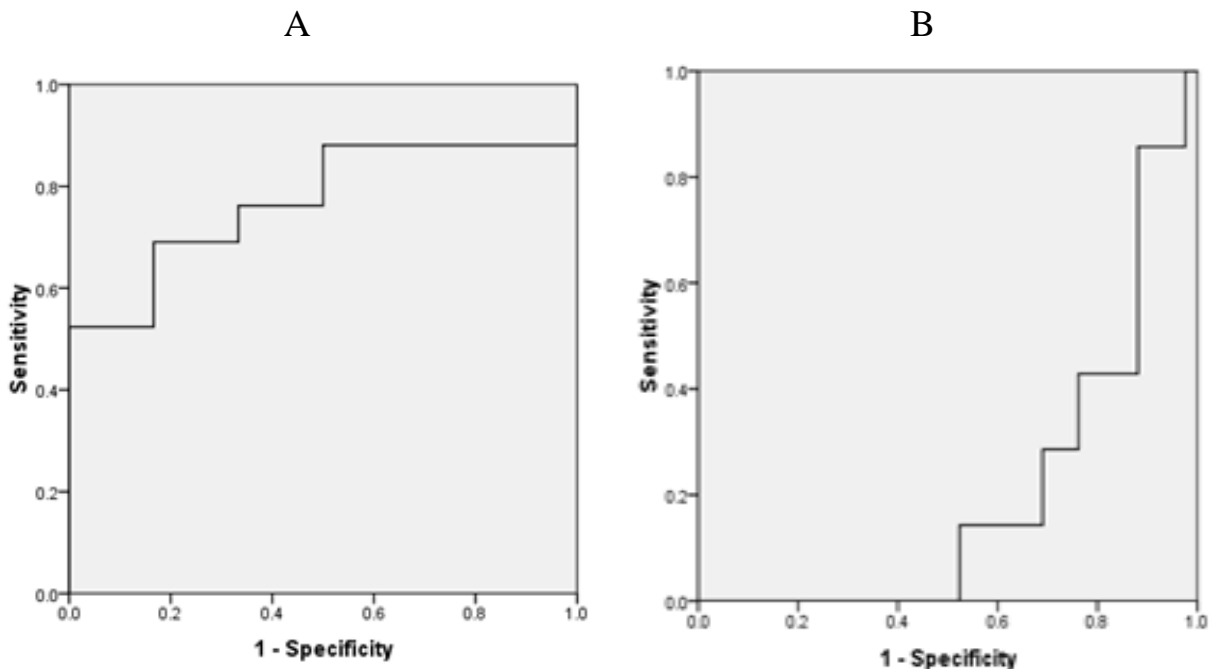
A   B

Fig (2): The Receiver Operator Characteristic (ROC) curve of portal vein blood flow volume (PVBF) for detection of fibrosis degree in liver biopsy. (A) For ≤F2, AUC was 0.77 (95% CI=0.622-0.917). At a cut-off point ≥ 0.443 L/min, portal vein blood flow volume had sensitivity of 76.2% and specificity of 66.7% in detecting hepatic fibrosis in liver biopsy is F2 or less. (B) For F3, it was not an accurate method (AUC = 0.201, 95% CI=0.61-0.340).
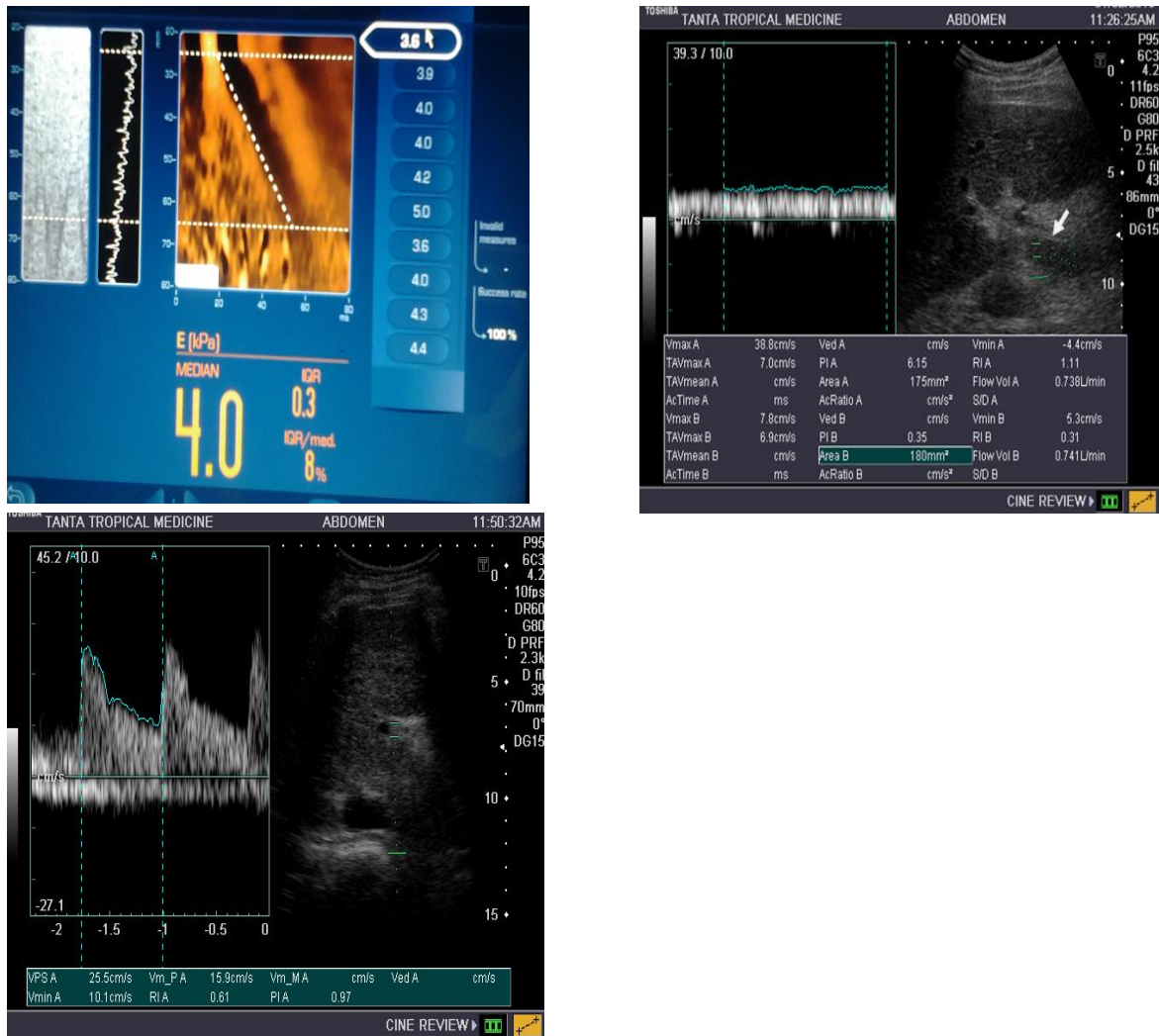
Fig. (3): Case 1 Doppler ultrasound of portal vein showing portal vein blood flow, and hepatic artery (resistive and pulsatility indices) and fibroscan of 32 years old female with F2 in liver biopsy.
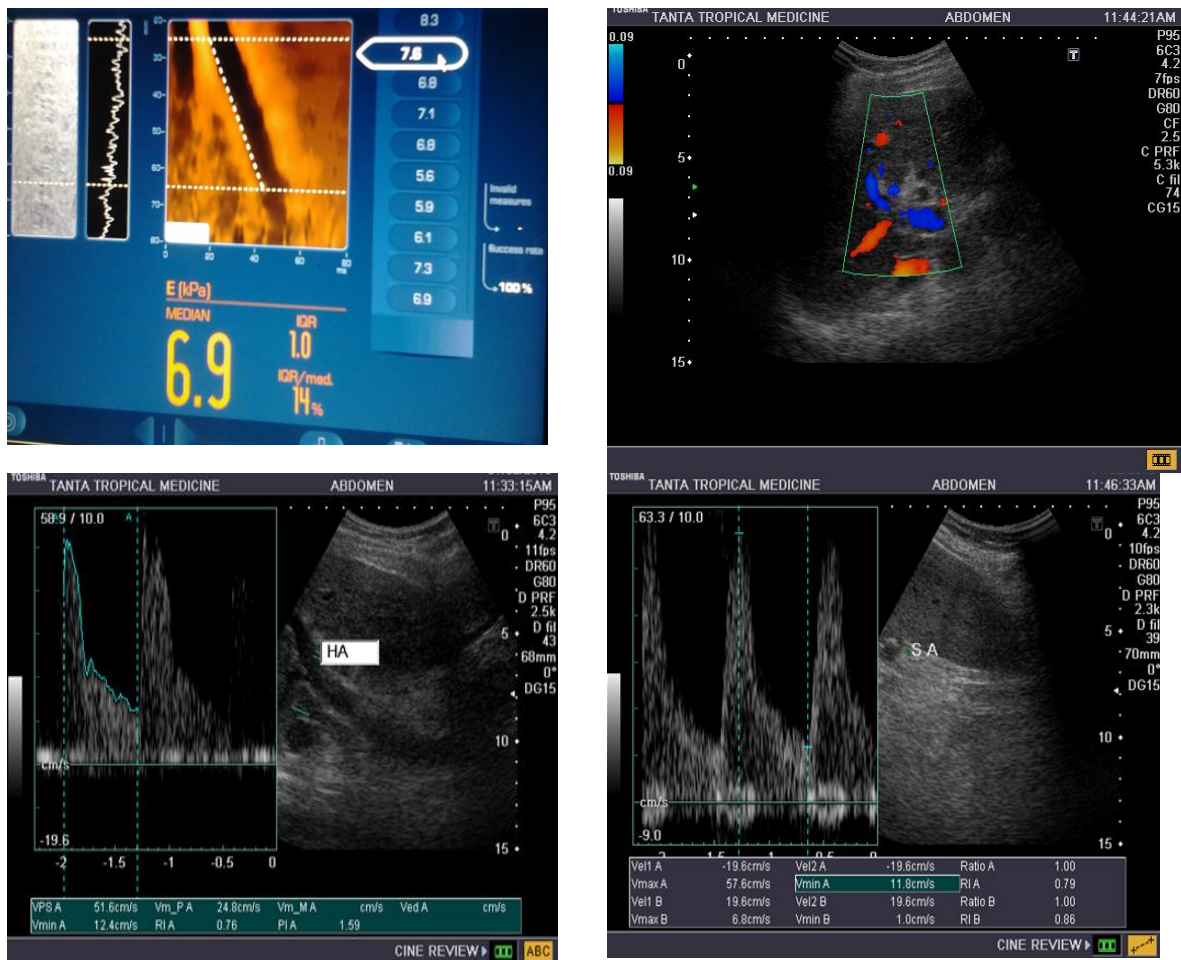
Fig. (4): Case 2: Doppler ultrasound of; portal vein showing hepatopetal flow, hepatic artery resistive and pulsatility indices, splenic artery resistive index and fibroscan of 38 years old male with F2 in liver biopsy.
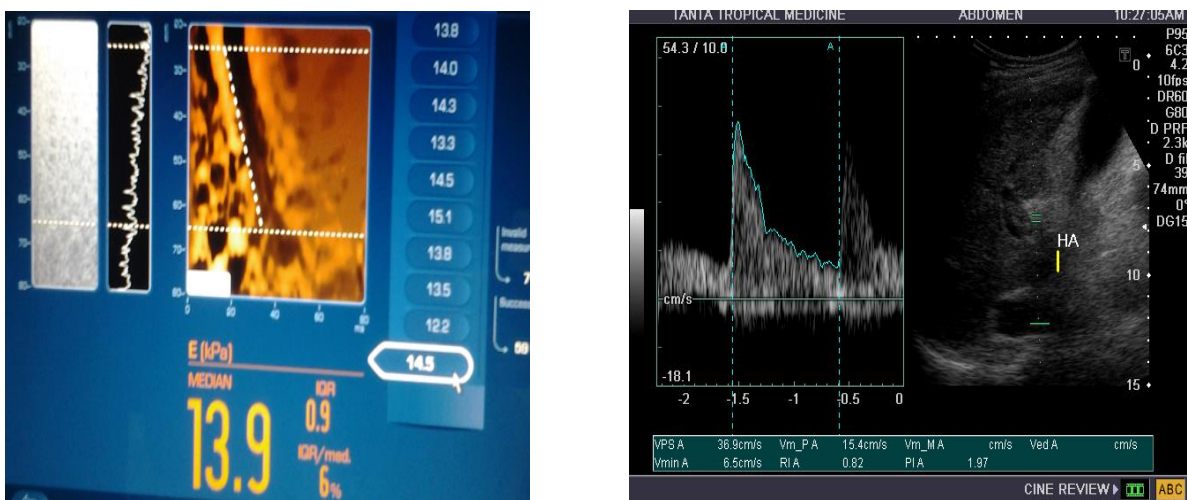

Fig. (5): Case 3: Doppler ultrasound of hepatic artery (resistive and pulsatility indices) and fibroscan of 54 years old female with F3 in liver biopsy.

DISCUSSION

In order to improve the efficacy of noninvasive evaluation of liver fibrosis , we compared Doppler ultrasound of hepatic blood flow and fibroscan: with liver biopsy in In Egyptian chronic hepatitis C patients. In all of the patients who were examined, a statistically significant positive correlation was observed between ultrasound findings and fibrosis score, liver biopsy, and fibroscan results as changes in liver echo pattern and texture were accompanied with increased estimated fibrosis levels in liver biopsy and fibroscan. This was similar to that obtained by Nishiura et al. (2005) who found that the increase of the texture of the liver parenchymal obtained by ultrasound has a statistically significant correlation with the degree of liver fibrosis [17].

Our results were also supported by the results of Abd El Dayem et al, (2013) who showed the diagnosis of hepatic fibrosis, by ultrasonography had 87.5% sensitivity, 77.5 % specificity, and 84.0 % accuracy, mainly significant fibrosis (F2-4). But, they concluded that ultrasound imaging cannot identify or precisely diagnose fibrosis in the absence of cirrhosis stigma, like shrunken liver and ascites [18]. It was also in agreement with Davoudi et al, 2015 who found a significant positive correlation between total their gray-scale score and liver fibrosis. They concluded that the liver parenchyma echogenicity may be enough and simple for use in clinical practice to detect fibrosis stage [19] Abd El Maksoud et al. (2015) have also, suggested that echo texture is significantly correlated with the level of fibrosis [20]. Choong et al. (2012), concluded that routine clinical ultrasound is not successful for liver fibrosis staging, giving treatment options , or determining the prognosis of chronic hepatitis secondary to chronic liver disease. They observed, however, that ultrasound is still beneficial for cirrhosis detection [21].

Fibroscan results revealed a strong positive association with the grade of fibrosis and activity index in histopathological analysis. Fibroscan was seemed to be more effective for F3 fibrosis diagnosis. To diagnose F3 fibrosis, we registered a 7.95 kPa fibroscan cut-off value.

Similar findings were obtained by several authors reporting distinct but nearby cutoff values such as Castéra et al, (2005) who reported a cutoff value of 9.5 for fibrosis prediction $\geq$ F3 with specificity 91% and sensitivity 73% [22]. In addition, Ziol et al. (2005) who stated a cutoff value of 9.6 for prediction of fibrosis $\geq$ F3 with specificity 85% and sensitivity of 86% [23]. Arena et al. (2008) who put cut off value of $\geq$ 10.8 for prediction of fibrosis $\geq$ F3 with specificity 94% and sensitivity 91% [24], This was similar to the results of Fahmy and Badran, (2011) who concluded that: With AUCs 0.92 and 0.95, TE is the most accurate tool for predicting severe fibrosis and cirrhosis and finding that with TE at 7 kPa, 86% were correctly classified for the prediction of significant hepatic fibrosis [25].

Similar to our results, Lutz et al. (2012) ROC analysis showed that in lower fibrosis stages Fibroscan lacks accuracy; and that there was a significant correlation between fibrosis degree detected by fibroscan and inflammation in the histopathological analysis [26]. The positive correlation between liver biopsy and the fibroscan score was also, concluded by Abd El Maksoud et al. (2015), with moderate agreement (matching) between liver biopsy and fibroscan, the lowest matching was in F0 and the highest was in F3 [20]. This was in line with El-Saadany S et al. 2016, who studied fibrosan and biopsy results in 348 CHC patients and found that fibroscan data in moderate fibrosis (p < 0.001) were positively correlated with biopsy, but not mild and no fibrosis (p=0.12) and concluded that fibroscan was correlated with fibrosis degree in liver biopsy and could be applied as a noninvasive tool for diagnosis moderate (F2– F3), but not mild (F1) fibrosis [27].

We tested Doppler US parameters as an indirect method for grading of hepatic fibrosis. All our patients had continuous hepatopetal blood flow, with a significant negative correlation between PVBF and fibrosis degree in liver biopsy and fibroscan score. These results may be attributed to the increased of hepatic parenchymal resistance that might be caused by fibrosis [28].

In 2002, Vyas et al. analyzed PVBF and PVV and observed that PVBF and PVV in cirrhotic patients were considerably lower than controls [29]. These changes increase as the liver disease gets rising, while Shi et al. (2005) who has observed 38 cirrhosis patients (Child grades A to C) and 20 controls showed that no variation in the diameter of the portal vein is obtained between controls and cirrhotic patients.

Portal flow for child C cirrhosis was significantly lower than for Child A and Child B cirrhosis, but no variations of PVBF was found among Child A and B cirrhosis patients and the controls **[30]**.

On the other hand Walsh et al. (1998) reported that portal vein flow and total hepatic flow were similar in chronic hepatitis C and controls (The indices of inflammation or degree of hepatic fibrosis were not linked to the state of the liver). These results may be due to the use of old fashion and inaccurate apparatus **[31]**. While 36 patients with chronic viral hepatitis, 30 patients without any signs of liver disease as a control group, and 63 patients with cirrhosis with no PVBF difference between three groups were observed by Haktanir et al. (2005), the PVD increased significantly and the mean PVV decreased significantly in cirrhosis compared with hepatitis and control groups **[32]**. One of the limitations of our study is a few patients with cirrhosis grade 4. The small sample size limits our ability to detect significant fibrosis if any. Also, the discrepancy between our results and the results obtained from studies that included cirrhotic groups may be due to increased hepatic inflow and decreased PVV mean these changes that accompany portal hypertension.

ROC curve analysis showed that PVB was more accurate in detecting lower grades of fibrosis than higher grades.

Normal hepatic artery RI was reported by McNaughton and Abu-Yousef, to be 0.55–0.7 [44], while normal hepatic pulsatility index was reported by Schneider et al, to be 0.92±0.1**[45]**.

There was a significant increase in mean values of HARI and HAPI in our patients compared to the normally documented values of HARI and HAPI in healthy subjects. These circulatory changes are considered to be occurring in patients with chronic hepatic disease in hepatic arteries are related to the architectural deterioration that occurs within the liver with greater severity of the disease **[33]**.

But there was no difference regarding HARI and HAPI between the two studied groups who had been categorized according to degree of fibrosis by liver biopsy, also there was no difference between HARI and HAPI between the two studied groups who had been categorized according to the degree of fibrosis by fibroscan, and there was no correlation between HARI or HAPI and the degree of inflammation in liver biopsy.

Our Results were similar to those found by Salvatore et al. (2012) who studied 100 patients who had a liver disease caused by hepatitis C, compared results of Doppler parameters with results of fibroscan for detection of the degree of liver stiffness and they found that in these patients HARI rises progressively compared to healthy subjects. They put a cut-off value of 0.64 for HARI at which Patients with LS values above 13 kPa with high sensitivity (84.4 %) and moderate specificity may be identified (69.1%), but finally, they concluded that fibroscan results were more accurate than Doppler parameters despite the direct correlation between HARI and liver stiffness **[34].**

Although Piscaglia et al. (2001) observed that HARI was higher in patients with severe hepatic fibrosis because the hepatic artery resistance indices seem to be influenced by inflammation and chronic repair that determine hepatic fibrous deposition, and secondly by aging **[35]**. On the other hand, Lutz et al (2012) observed that HARI did not display any substantial variations in fibrosis scores F1-F3 but was significantly higher in cirrhosis, although no statistically significant differences in HAPI measurements in the various stages of fibrosis (F0-F4/cirrhosis) was found **[26]**. In comparison, Lim et al. (2005) did not find an association between HARI values and histological scores **[36]**.

The normal value of splenic artery resistive index (SARI) was reported by Loanitescu to be 0.51 +/- 0.05 **[46]**.

A significant increase in the mean value of SARI measured among all patients in our study was found compared to normally documented values, this difference may be explained as the advance of hepatic fibrosis contributes to increased portal resistance, which induces increased resistance to splenic artery outflow**[37]**.

But our results did not find any significant differences among the studied groups and there was no correlation between SARI and fibrosis score neither to liver biopsy nor fibroscan results.

Similar to our result Liu et al, (2007) documented that SARI and SAPI were correlated with the degree of fibrosis **[38]**.

Results in this work were different from that obtained by Salvatore et al. (2012) who found that there was a direct correlation between SARI and liver stiffness taking into consideration that

the study was restricted to the TE values for F ≤ 2. The SARI cutoff value of 0.56 was used to detect patients with LS values >13 kPa with strong sensitivity (81.3%) and moderate specificity (48.5%). However, they concluded that despite the significant correlation between LS and Doppler US parameters, they were not excellent in detecting liver stiffness **[34]**.

While Cançado et al. (2007) found that the results of SARI were similar in patients with chronic hepatitis and healthy individuals, but it was established that patients with cirrhosis had greater indices **[39]**.

We also measured the hepatic vein resistance index of the right hepatic vein (HVRI) and there was no significant difference between the two studied groups and there was no correlation with fibrosis score in liver biopsy or in fibroscan results (p > 0.05). as far we know, the only study conducted with the estimation of HVRI by Lutz et al. (2012) who studied 125 patients (with different grade of fibrosis from F0 to F4) the results showed that HVRI associated with the stage of fibrosis showed the patients without fibrosis exhibited uppermost scores and no significant difference between the different stages of fibrosis was noticed and that HVRI could detect fibrosis of the F2 or higher stages, but it is of limited value in detecting mild fibrosis and that it has superior sensitivity and specificity than fibroscan and HVRI values were not affected significantly by different stages of inflammation or steatosis. This difference may be due to the difference in the study population as they included patients with mixed causes of hepatic cirrhosis while in our result we included only HCV- infected patients who were not cirrhotic **[26]**.

The limitation of the study: this was a retrospective study that leads to losing of some records and data .so numbers of cases in our study were less; and it was a single center study.

CONCLUSION

Fibroscan has a good matching with liver biopsy in the detection of higher grades of fibrosis and it lacks accuracy in detecting lower grades of fibrosis. Fibroscan results were affected by grade of inflammation in liver biopsy which may cause overestimation of grade of fibrosis. However, Doppler US is more sensitive in detecting lower grades of fibrosis than higher grades in HCV infected patients.

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