Role of Transient Elastography in Early Detection of Hepatocellular Carcinoma in Cirrhotic Patients

Hanaa A. Baddour, Hesham E. El Sheikh, Ahmed E. shalan

Department of radiology, Benha faculty of medicine, Benha University, Egypt.

Correspondence to: Hanaa A. Baddour Department of radiology, Benha faculty of medicine, Benha University, Egypt.

Email:

hermy_bloody@yahoo.com

Abstract

Background: Hepatocellular carcinoma is the most common primary malignancy of the liver and one of the most frequent causes of death in patients with liver cirrhosis. In Egypt it is one of the most challenging tumors with high incidence, prevalence and mortality rates. The degree of liver fibrosis is the strongest indicator of risk for HCC development that is why liver stiffness measured by TE is useful in demarcating patients at a high risk for HCC, who require frequent check-up by imaging examinations. **Aim of work:** The aim of this study was to study the role of US elastography (FibroScan) in early detection of HCC in cirrhotic patients in comparison with triphasic CT. **Patient and methods:** This study was conducted on 100 patients with liver cirrhosis, 50 of them had HCC. The entire patients were diagnosed with liver cirrhosis by US examination and underwent fibroscan to estimate the degree of fibrosis and then triphasic CT to confirm or exclude the presence of HCC. **Results:** There is a correlation between high TE results and the incidence of HCC detection by CT, HCC detection was (100%) in the groups with LSM value (>30KPa) and low (9.6%) in the group with LSM value (15-25KPa). **Conclusion:** The higher LSM, the more liability for the patient to have HCC on CT scanning.

Keywords: Hepatocellular carcinoma, transient elastography, triphasic CT, liver stiffness measurement.

Introduction

HCC is a primary malignancy of the hepatocyte, the major cell type in the liver (1) Ultrasonography is the least expensive choice for screening, but it is highly operator-dependent. A suspicious lesion on a sonogram generally requires additional imaging studies to confirm the diagnosis and the stage of the tumor (2). The elasticity of a body is defined as the ability of the body to deform itself under the action of a mechanical force.

The elasticity of a tissue can be estimated on the basis of the speed of propagation of wave. The higher the speed of propagation of that wave, the higher the stiffness of the tissue. Transient elastography (TE) measures such speed of propagation in relatively homogenous organs such as the liver, by using ultrasound (US) pulses to localize the shear elastic wave at different times (3).

Patients and methods

This prospective study was conducted between February 2018 to March 2019 on 100 patients with cirrhosis who visited Gastrointestinal Surgery Center of Mansoura University and gave their informed consent after approval of the institutional ethical committee. Fifty patients had cirrhosis with HCC diagnosed by US and confirmed by triphasic CT study and patients 50without evidence of HCC diagnosed by clinical, laboratory, US and confirmed by triphasic CT study.

The diagnosis of liver cirrhosis was done by US examination, then we performed fibroscan to these patients, either these patients had cirrhosis on US examination or not. Then triphasic CT was done to confirm liver cirrhosis and the presence of HCC.

Transient Elastography Liver stiffness measrment (LSM) was performed using Fibroscan, General Electric LOGIQ E9 (LE9) scanner with 2D shear wave elastography on a conventional ultrasound scanner. A time aligned sequential tracking (TAST) technique that enables high pulse repetition frequency (PRF) shear wave tracking on conventional ultrasound scanners was implemented with the Comb-push Ultrasound Shear Elastography (CUSE) technique on the General Electric LOGIQ E9 (LE9) scanner and combined to realize large field-of-view (FOV) 2D shear wave elastography. The elastic wave propagates through the underlying tissues the stiffer the tissue, the faster the shear wave propagates.

The median value of ten successful acquisitions expressed in kilopascal (KPa) and was kept as representative of liver stiffness measurement. The clinical interpretation of TE depends on two important parameters for results to be considered reliable:

- The success rate (the ratio of the number of successful measurements to the total number of acquisitions) should be at least 60%.
- IQR/Median (the coordination between different measurements)

- Results were expressed in kiloPascals (KPa) and 10 validated measurements were recorded for each patient (4).

The degree of fibrosis measured by TE correlated with the presence of HCC or not by triphasic CT scan.

liver stiffness measured noninvasively by TE has been reported to be well correlated with histologically assessed liver fibrosis stage (5).

Results

There was no statistical significant difference between the groups as

regards the age, sex or smoking; however HCC tends to be more common in males than females. Also, HCC tends to be more common in urban areas than rural areas and more common in farmers than non-farmers.

Hard liver was significantly common in HCC group. There is no statistical Most of cases were Okuda stage III, CLIP stage II, VISUM stage I and advanced Tokyo staging.

There was no statistical significant difference between the groups as regards the severity of liver cirrhosis assessed by MELD and uMELD scores however; they tend to be higher in HCC group.

difference between the two groups as regards the frequency of hepatomegaly or splenomegaly.

Platelet count, RBCs count and albumin were significantly lower in HCC group. ALT, AST, ALP, INR and serum bilirubin were significantly higher in HCC group. Prothrombin time was significantly prolonged in HCC group.

There was no statistical significant difference between the groups as regard fasting blood sugar, hemoglobin, WBCs or s. creatinine; however s. creatinine tends to be higher in HCC group.

All studied patients of both groups were HCV Ab. positive and none of them were HBsAg positive.

Alpha fetoprotein levels were significantly higher in HCC group.

Most of patients of HCC group were Child C rather than Child A & B.

All patients were cirrhotic; most of them had shrunken liver (42%) and splenomegaly (94%). Ascites was found in 22%, 34% had portal hypertension, 8% had esophageal varices and only 14% had portal vein thrombosis.

PVT was found in 10% of patients. Focal lesions by CT tend to be single, more in

Right lobe, ≥5cm in diameter. 10% of patients had enlarged lymph nodes and only 6% with hepatic vein involvement.

CT was superior in detection of both lymph nodes and hepatic vein involvement.

Liver stiffness and Inter Quartile Range measured by Fibroscan were significantly higher in HCC group. But, there was no statistical significant difference between the groups as regard the success rate (Fig1).

There is a correlation between high TE results and the incidence of HCC detection by CT, HCC detection was (100%) in the groups with LSM value (>30KPa) and low (9.6%) in the group with LSM value (15-25KPa) (Fig 2)

It was found that likelihood of HCC risk was correlated with increase of liver stiffness. At liver stiffness of <25 KPa, the probability of HCC presence was about 72% while stiffness of 25-30 KPa has a probability of 91% so, these patients should undergo close follow up.

Patients with stiffness ≥30 KPa had HCC.

There was significant positive correlation between liver stiffness by fibroscan and Child – Pugh, tumour size, Okuda

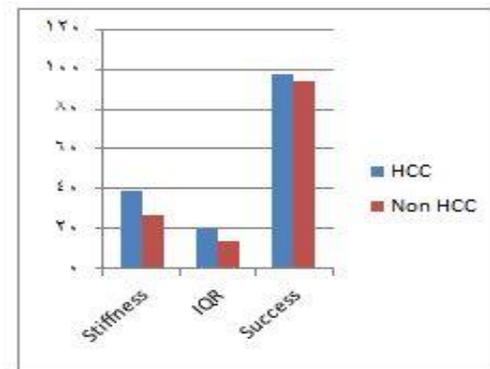classification, CLIP staging and Tokyo classification among HCC patients.

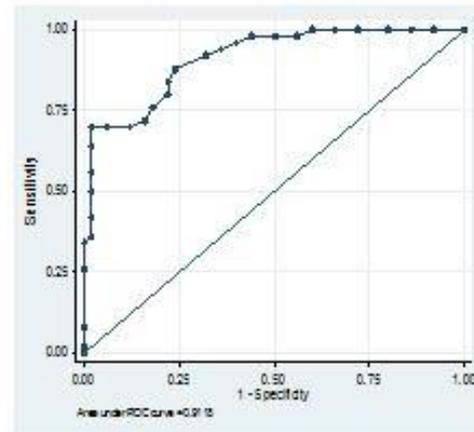Figure (1) Fibroscan results of the studied patients.

Figure (2) ROC curve analysis of Stiffness in prediction of hepatocellular carcinoma.

Discussion

In this study 100 patients were included, 50 patients with liver cirrhosis and did not had HCC, and 50 patients were cirrhotic and had HCC, patients with HCC had a mean age of 53.5 years with a range between 44-68 years old, while cirrhotic non-HCC patients are younger

with a mean age of 51.3 years and ranging between 39-67 years old (6).

HCC commonly presented in males more than females with a male to female ratio 5.2:1(7) and 58% of HCC cases were from urban areas (8)

The current study showed that 56% of HCC cases had a history of smoking (9). There was a traditional conflict about the link between cigarette smoking and the occurrence of HCC (10). But recent evidence support that smoking is a clear co-factor (11). In HCC patients, hepatomegaly and hard liver were observed in many patients (12).

Most of manifestations of decompensated liver cirrhosis such as ascites, jaundice, lower limb edema, hepatic encephalopathy that are common findings in chronic liver disease without HCC, are not useful in early suspicion or diagnosis of HCC comparing to cirrhosis (13).

AFP is the most commonly used biomarker for patients at risk for HCC (14). AFP in HCC cases had a mean value of 627.6ng/ml which was statistically higher than that of patients with cirrhosis 11.7ng/ml.

Most of the patients with HCC (64%) were Child C, followed by Child B (20%) then Child A (16%) (9).

According to MELD and uMELD scores, in this study the mean scores for patients with HCC were 20.6 and 4.2 respectively, while the mean scores for patients with cirrhosis were 19.9 and 4.08 respectively(15).

US is very effective in early diagnosis of HCC as it can detect about 76% of early HCC patients (16). It is a good tool for HCC detection with a sensitivity of about 80% and specificity of over 90%. Abdominal US was done to evaluate the liver status in the studied patients and all of the patients (100%) with HCC had sonographic evidence of liver cirrhosis. By US examination, five patients (10%) in this study were found to have portal vein thrombosis.

Twenty six patients, representing 52% of HCC cases had single focal hepatic lesion, while two focal lesions and multiple hepatic focal lesions were present in eight (16%) and sixteen (32%) of cases respectively (17).

In our study we observed that 18 (36%) of HCC patients had their tumour size less than 5cm while 32 (64%) had their tumour size more than 5 cm (15), while the right lobe was predominantly more affected by tumour (54%) than left lobe (10%) and both lobes (36%) (18). Five

patients (10%) of HCC cases were found to have lymph node enlargement (19).

As regard Okuda staging, most of HCC cases were in the late stage; stage III (46%), followed by stage II (38%) then stage I (16%) (20).

According to CLIP staging, most of HCC cases were presented at the intermediate stage II (62%) comparing to the patients presented at the early stage (10%) and the advanced stage (28%) respectively (20).

According to Tokyo staging, most of HCC patients were presented at advanced stage (58%) comparing to the patients presented at early stage (42%) (21).

The important observation in our study is that most of patients are diagnosed at advanced stages so; there must be a screening program for early detection of the patients with HCC.

When we used ROC curve, the cutoff value for HCC was 30.4 KPa with sensitivity of about 72% , specificity about 84% , positive predictive value about 81.82% and negative predictive value about 75%(22).

There was a positive correlation between the liver stiffness & the presence of HCC. Also, prediction of occurrence of HCC by fibroscan may be of useful value. SSLR for HCC presence by liver stiffness was

0.7272 in <25 KPa, 0.9167 in 25.1 to 30kPa, 1.00 in 30.1 to 35 KPa, 1.1428 in 35.1 to 40kPa and 1.3333 in >40 KPa, so there is a direct correlation between high degree of LSM by TE and detection of HCC in cirrhotic patient by triphasic CT. Patients who had high LSM> 30 KPa was proved (100%) to had HCC by CT, while patients with LSM <25 KPa was found to had HCC on CT scanning with a percentage 72% and almost all the patients in our study that did not had HCC on CT scanning had LSM between 15-25 (23).

Also there was direct correlation between the size of the tumor and stiffness measured by fibroscan. The bigger the size of the tumor; the higher the stiffness (24).

We noticed that there is a direct correlation between Okuda classification, CLIP staging and Tokyo classification with the stiffness measured by fibroscan. The more advanced liver disease (according to each classification); the higher stiffness of fibroscan.

In spite that liver biopsy is the gold standard diagnostic tool to compare with in our study for detection of hepatic focal lesions and incertitude about their nature rather than triphasic CT, its' invasive painful interventional nature was a

limitation that stimulated the search for noninvasive approaches but we recommend using biopsy as a gold standard modality in spite of triphasic CT to confirm the diagnosis of HCC for its certainty.

Our study was conducted on a small sample volume, so it needs to be applied on a large sample volume to be more reliable.

The final diagnosis was done using triphasic CT not biopsy as a gold standard diagnostic tool, which is known to be the most confirmative for diagnosis.

Conclusion

The results show that the higher LSM the more liability for the patient to have HCC on CT scanning.

Also there was direct correlation between the size of the tumor and stiffness measured by fibroscan. The bigger the size of the tumor; the higher the stiffness.

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