

DIAGNOSTIC ACCURACY OF HEPATIC TUMOR INDEX ON DOPPLER SONOGRAPHY FOR THE DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

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ABSTRACT

Objective: The purpose of this study was to determine the Diagnostic Accuracy of Hepatic Tumor Index (HTI) on Doppler Sonography for the diagnosis of Hepatocellular carcinoma (HCC) while differentiating it from other very closely resembling pathologic lesions like Metastases and Hepatic hemangiomas.

Material and Methods: The study was held in the Department of Diagnostic Radiology, Lahore General Hospital, Lahore. All patients included in the study were within the ages of 20-70 years and from both genders who attended indoor and outpatient departments from June 2012 to June 2013. Color Doppler Ultrasonography (CDUS) was done on 105 patients with irregular hepatic lesions less than 03 cm in diameter. The HTI was estimated as the ratio of the tumoral peak systolic velocity (PSV) to the PSV of the right or left hepatic artery. The results of Doppler Sonography and Histopathology were compared taking Histopathology as gold standard.

Results: Out of 105 positive cases, the HTI was 1.0 or greater in 91 cases suggesting that those patients had hepatoma while HTI was less than 1.0 in 14 cases suggesting such patients to be harboring tumors other than hepatocellular carcinoma (HCC). Hence in hepatic lesions a tumoral PSV equal to or greater than 0.40 m/sec and HTI equal to 1.0 or greater was related with 97.78 % sensitivity, 80% specificity, 96.70 % positive predictive value, 85.71 % negative predictive value and 95.23 % diagnostic accuracy in differentiating HCC from hepatic metastases and hemangiomas.

Conclusion: The HTI on CDUS is useful in differentiating HCC from other hepatic lesions especially hepatic metastases or hemangiomas. We strongly recommend CDUS for the evaluation of HCC because it is highly accurate, easily available and non-invasive imaging modality for its diagnosis.

Keywords: Hepatocellular carcinoma, Positive predictive value of Doppler Sonography in Liver tumors.

INTRODUCTION

Hepatocellular carcinoma (HCC) also called as "hepatoma" is cancer of the liver¹. There are great regional differences in the epidemiology and pathology of the condition². Males are affected more than females. It is most commonly seen between the ages of 30 to 50³. The disease is commoner in Asia and Africa compared with other parts of the world and is considered endemic to those regions^{4,1}. Infection of the liver by chronic hepatitis B virus (HBV) is the primary risk factor for HCC, although its etiology has also been linked to environmental, dietary and lifestyle factors⁵. As in the case of HBV infection, chronic hepatitis C is also an important risk factor for HCC^{6,3}. 27% cases of cirrhosis and 25% cases of HCC worldwide are estimated to occur in HCV-infected people⁷. The two major sources of toxins that contribute to HCC development include

alcohol and aflatoxin^{8,9}. Other toxins causing HCC include genetic hemochromatosis, porphyria cutanea tarda, tyrosinemia, hypercitrullinemia, alpha-1 antitrypsin (AAT) deficiency and Wilson disease¹⁰.

Malignant focal liver lesions are quite frequent, most common being metastases from other organs¹¹. Imaging plays an important role in cases suspected to be having hepatic malignancy, not only for making a diagnosis but also for staging the disease. The Triple-phase helical CT and triple-phase dynamic contrast enhanced Magnetic Resonance Imaging (MRI) are considered to be most reliable diagnostic tests. However the accuracy for lesion detection by CT and MRI is somewhat affected if the lesion size is less than 2cm¹². Biopsy is rarely required for its diagnosis^{13,12}. Ultrasound is generally a fundamental technique for imaging the liver, biliary tree and gall bladder¹⁴.

Application of Color Doppler Ultrasonography (CDUS) is useful in the detection of intra-tumoral vascularity. Hepatoma displays pattern of fine branches of increased vascular flow with PSV greater than that in hemangiomas or metastatic lesions. CDUS of portal vein can help in differentiating bland thrombus from tumor invasion by revealing vascularity in the malignant thrombus. Malignant portal vein invasion usually displays arterial waveform¹⁵. Recently CDUS has been used to characterize focal hepatic lesions with an even higher diagnostic yield. A PSV of greater than or equal to 0.40 m/sec suggested a malignancy of liver rather than hemangiomas with 67% sensitivity, 91 % specificity and 71 % diagnostic accuracy. However, measurement of tumoral PSV failed to differentiate HCCs from hepatic metastases. On CDUS, sensitivity of 76%, specificity of 92% and 82% Diagnostic accuracy in differentiating HCC from liver metastatic lesions has been documented. In hepatic tumors, PSV equal to or greater than 0.40 m/sec and HTI equal to 1.0 or greater was associated with sensitivity of 91 % , specificity of 83% and diagnostic accuracy of 89% in differentiating HCC from hepatic metastatic lesions^{16,17, 18}. In a recent study conducted in 2011, the positive predictive value of CDUS was 92% for diagnosing hepatoma in chronic liver disease patients¹⁹. CDUS is more practical than other imaging modalities because it is safe, cheap and non-invasive technique for the diagnosis of HCC. The present study is an effort to use Hepatic Tumour Index as a guide to assess the nature of hepatic lesion so that the need for the biopsy may be averted and a confident diagnosis could be made without any intervention for initiation of treatment.

MATERIAL AND METHODS

The study was conducted in the Department of Diagnostic Radiology, Lahore General Hospital, Lahore for a period of 13 months from June 2012 to June 2013. The study group comprised all patients who fulfilled the inclusion criteria. These patients were enrolled in the study from OPD as well as Indoor of the same hospital. Inclusion criteria were age from 20 to 70 years, Hepatic lesions less than 3 cm in size with irregular contours and hepatic tumoral peak systolic velocity equal to or greater than 0.40 m/sec on CDUS. Patients with known primary carcinoma other than that of the liver, biopsy confirmed metastatic liver lesions, with history of previous surgery for malignancy and recurrent cases of liver lesion(s) were excluded from this study. By using convex probe of 2.5 to 3.5 MHz frequency (ESOATE, Mylab 20 plus ultrasound system, Holland) scanning of patients was done at Department of Radiology, LGH, Lahore by researcher and the co-authors. After

obtaining informed consent, patients fulfilling above mentioned criteria underwent CDUS. HTI was calculated as the ratio of tumoral PSV to the PSV of left or right hepatic artery. For lesion in the right lobe, arterial velocity was estimated from the right Hepatic Artery and vice versa. Angle of insonation was kept at 60 degree or close to it but was not made to exceed 60 degree in order to maintain uniformity of standard of calculations. All basic demographic information of each patient (Name, age, sex, address and contact number) was also obtained. The biopsy acquisition was done under ultrasound guidance using free hand technique through fine needle aspiration in patients who had been labeled positive on CDUS. The obtained specimen was sent to the Department of Pathology for histopathologic examination. The reports of histopathology were assessed for the confirmation of positive and negative cases. All the information was recorded through pre-designed performa.

RESULTS

The study was conducted on 105 patients with tumoral peak systolic velocity equal to or greater than 0.40 m/sec on color Doppler Sonography during this period of 13 months. Following observations were made at the end of the study period.

Most common age group was 20-40 years and least patients were between 61-70 years. Mean age of the patients was 49.7±7.4 years.

Out of 105 patients, 68 patients, (64.7%) were males while 37 patients (35.3%) were females.

The HTI was equal to 1.0 or greater in 91 cases thereby rising suspicion of hepatoma while it was less than 1.0 in 14 cases suggesting that those patients had tumors/lesions other than hepatoma.

So 91 tumors had HTI equal to 1.0 or greater. Out of them 88 were proven to be HCC while 03 were metastatic tumors/ hemangiomas. There was not a single case of hemangioma falling in this category. According to Hepatic Tumor Index on CDUS, 88 cases were true positive, 02 were false negative, 03 were false positive and 12 were true negative as confirmed by histopathology reports. Hence in hepatic lesions a tumoral PSV 0.40 m/sec or greater and HTI 1.0 or greater was associated with sensitivity 97.78 % , specificity 80%, 96.70 % positive predictive value (PPV), 85.71 % negative predictive value (NPV) and 95.23 % diagnostic accuracy in distinguishing HCCs from hemangiomas and liver metastases.

DISCUSSION

HCC is the primary malignancy of liver. Most of cases are secondary to viral hepatitis (hepatitis B or C) or

hepatic Cirrhosis (Alcoholism being the most common cause of cirrhosis). It is most commonly diagnosed by ultrasound due to its cost effectiveness and easy availability. Other methods include the measurement of serum alpha protein in combination with the triple phase CT/MRI. The prognosis of such patients is usually poor. Only in few percent of cases, the lesion can be resected completely. If resection is not possible, the patients usually die within 3-6 months.

In our study, age range of the patients is 20-70 years with mean age of 49.7 ± 7.4 which is in accordance with literature which states that the most common age range for HCC is 30-50 years. Tumoral PSV equal to or greater than 0.40 m/sec along with an HTI of 1.0 or greater was associated with 97.78 % sensitivity, 80% specificity, 96.70 % PPV, 85.71 % NPV and 95.23 % diagnostic accuracy in differentiating hepatomas from liver metastases and hemangiomas which is in accordance with literature which states that HTI equal to 1.0 or greater compatible with 91 % sensitivity 83% specificity and 89% accuracy in differentiating HCCs from hepatic metastases¹⁸. Lin et al in their study demonstrated PPV of CDUS in detecting HCC to be 96.4%²⁰. This figure is comparable with our results. Tong et al reported the PPV for CDUS to diagnosis HCC to be 78%, while sensitivity and specificity were 100% and 98%, respectively²¹. Larcos et al demonstrated that Alpha-fetoprotein (AFP) should not be used as only test for screening and surveillance for HCC because of its PPV and low sensitivity. Larcos et al also demonstrated that ultrasonography screening should be used in conjunction with AFP assay for detection and follow up of HCC²². Furthermore, when the tumoral peak systolic velocity was equal to or greater than 0.4 m/sec, the hepatic tumor index value was associated with an accuracy of 95.23% in distinguishing HCCs from metastases. Both cases of hemangiomas in our study had a hepatic tumor index of less than 1.0. Hemangiomas are hypervascular tumors in which normal-caliber arteries taper and subdivide normally into small vessels²³.

Numerous studies have been conducted on the gray scale ultrasound reflecting structural characteristics of hepatic tumors. However, gray-scale sonography has limitations in distinguishing advanced HCC from metastatic disease. In such cases, the HTI using CDUS may be useful to differentiate the tumors¹⁸. In the present study, an HTI equal to 1.0 or greater was associated with an accuracy of 95.23 % implying that this index can be useful in differentiating HCCs from metastases as well as hemangiomas.

The present study did not incorporate gray-scale data in the differentiation of hepatic tumors. To improve

the accuracy of the differential diagnosis of HCCs versus metastases / hemangiomas, further studies are indicated on the use of the HTI combined with the characteristics of the gray-scale sonogram.

Size as well as depth of the tumor are known to effect the sensitivity of the pulsatile imaging in CDUS. Similarly the angle of incidence of ultrasound beam with respect to blood vessels as well as attenuation of the ultrasound beam as it traverses through the cirrhotic parenchyma are also known to effect the sensitivity. Hence for obvious reason is difficult to carry out in all cases. However, we believe that the HTI using CDUS is helpful in differentiating HCCs from metastatic lesions.

CONCLUSION

It is concluded that Color Doppler Sonography is a highly effective means for diagnosing HCC as it is widely available, cost-effective, quick, safe and non-invasive imaging modality. As compared to CT scan, it is safe in terms of lack of radiation exposure. Doppler Sonography not only provides reliable information regarding the location and characterization of hepatic lesion but also aids in detecting its associated complications like portal vein thrombosis etc. in the simplest way. Moreover, due to its real time benefit, biopsy of lesion can be done easily, most of the times in the same sitting. Therefore HTI using CDUS is helpful in differentiating HCCs from other tumors especially metastatic lesions and hemangiomas. The author wishes to stress upon the assessment of every hepatic lesion using CDUS, which in expert hands, is very likely to make a certain reliable diagnosis of Hepatoma. Hence need for biopsy may be averted in the majority of cases and consequently treatment may be initiated without any delay.

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