Role of Diffusion Weighted Imaging (DWI) for Hepatocellular Carcinoma (HCC) Detection and its Grading on 3T MRI: A Prospective Study

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Background: **Limited studies have evaluated the role of diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) for histologically grading the hepatocellular carcinoma (HCC).** ***Objective:*** **To compare the efficacy of DWI with dynamic contrast enhanced magnetic resonance (DCEMR) in detection of HCC in cirrhosis, and to evaluate whether DWI can be used instead of DCEMR.** ***Methods:*** **20 patients of either sex with cirrhosis and suspected of having HCC on screening USG were included in this prospective study approved by the Institutional Ethics Committee. All patients underwent DCEMR of the abdomen on 3T scanner and fine needle aspiration of the lesions. MR protocol included T1WI, T2WI, DWI, and dynamic CEMR. The results of diffusion weighted imaging were compared with DCEMR to find the efficacy of DWI vis-à-vis CEMR.** ***Results:*** **DWI had a sensitivity and specificity of 100%, for diagnosis of lesions in cases having single lesion on CEMR, and sensitivity of 75% and specificity of 100% for diagnosis of lesions in cases having multiple lesions. There was a decreasing trend of ADC values with increasing grade of the tumor; however, the decreasing trend was not statistically significant. A cut-off ADC value of 0.8705 resulted in a sensitivity of 75% and specificity of 50% for differentiating between well-differentiated and other grades of HCC.** ***Conclusion:*** **DWI can be used as an alternative for the detection and characterization of HCC, especially in patients with impaired renal function or contrast allergies precluding the use of contrast. In addition, DWI with ADC measurement may be helpful for non-invasive and preoperative prediction of the degree of differentiation of HCC. (J Clin Exp Hepatol 2016;6:303–310)**

Hepatocellular carcinoma (HCC) is the sixth most commonly encountered cancer worldwide and third most common cause for the cancer-related death globally. It is the most common primary hepatic malignancy with around 80% cases developing predominantly in patients who have underlying cirrhotic background.[1–4] Arterial phase enhancement is considered as the essential characteristic of HCC and dynamic contrast enhanced magnetic resonance (DCEMR) imaging is considered as the gold standard for the diagnosis of HCC non-invasively.[5] Patients having impaired renal function or history of contrast allergies cannot be administered gadolinium contrast agent for DCEMR, and hence an alternative imaging technique is required for the detection and characterization of HCC.

Diffusion weighted MR imaging (DW-MRI) has emerged as a non-invasive sequence which works on microscopic motion of water in tissue. It is being increasingly used in liver diseases due to availability of echo-planar imaging and parallel imaging techniques which has considerably improved the quality of images with reduction of artifacts related to breathing, cardiac motion, and bowel peristalsis.[6] Even though previous studies have reported DWI to have improved sensitivity when combined with CEMR in diagnosing HCC, to the best of our knowledge, there is no previous prospective study directly comparing the efficacy of diffusion weighted imaging (DWI) against DCEMR in the diagnosis of HCC on a 3T MRI scanner. Among the several forecasters of recurrence of HCC after surgical resection, histological grading is the most important foretelling factor for early tumoral recurrence.[7,8] Hence, preoperative prediction of grade of tumor may be helpful for clinicians for further management. It has been hypothesized that highly cellular tumors are associated with more restriction of motion of water molecules,

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Abbreviations: ADC: apparent diffusion coefficient; DCEMR: dynamic contrast enhanced magnetic resonance; DWI: diffusion weighted imaging; HASTE: half-Fourier acquisition single-shot turbo spin echo; HCC: hepatocellular carcinoma; TSE: turbo spin echo; VIBE: volume interpolated breath hold examination
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and hence apparent diffusion coefficient (ADC) values are considerably lower for malignant lesions compared to lesions of benign nature and also for high grade tumors than for low grade tumors.[6,9]

Limited studies have evaluated the role of DWI and ADC for histologically grading the HCC. However, they have revealed contradicting results for correlation between grade of HCC and ADC values. Hence, the results at present are equivocal for correlation of ADC values with tumor grading. Thus, in the present study, DWI efficacy was compared with DCEMR in detection of HCC in cirrhotics, taking DCEMR as gold standard. We also evaluated whether DWI can be used instead of DCEMR. This can avoid the use of intravenous contrast which will be more beneficial to patients with hepatic and renal failure. The correlation between calculated ADC values and grades of tumor was also looked for, and cut-off ADC value for various grades of HCC was looked for.

MATERIALS AND METHODS

The prospective study was approved by the Institutional Ethics Committee of Post Graduate Institute of Medical Education and Research, Chandigarh, India. Informed written consent was obtained from all patients. The fine needle aspirate of the focal hepatic lesions was also approved, as we needed to grade the lesion as a part of the study protocol.

Study Population

A total of 20 patients of either sex who presented to outpatient department (OPD) of hepatology clinic of our institute over a period of 18 months, with chronic liver disease and suspected of having HCC on screening USG were included. None of them had undergone previous locoregional therapy or surgery for the liver lesion.

These twenty patients (19 men and one female) were in the age range of 40–80 years with a mean age of 59.05 years. The underlying cause of cirrhosis was HBV in 9 patients, HCV in 6 patients, alcoholic cirrhosis in 4 patients, and non-alcoholic steatohepatitis (NASH) in one patient. The mean AFP level in the study group was 80.13 ng/ml with 14 patients having AFP levels less than 100 ng/ml.

Imaging Protocol

MR abdomen was done on 3T (SIEMENS VERIO) imaging system using a body coil. The protocol included T1 weighted axial imaging, T2 weighted axial imaging including both non fat suppressed and fat suppressed sequence, axial DWI and conventional axial DCEMR. The T1-weighted gradient echo sequence had following parameters: TR—120 ms, TE—2.46 ms, flip angle—65°, slice thickness—6 mm, interslice gap—1 mm, matrix—320 × 320, and field of view—38 × 38 cm. The T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) sequence had following parameters: TR—2000 ms, TE—96 ms, flip angle −150°, slice thickness—6 mm, interslice gap—1 mm, matrix—320 × 320, and field of view—38 cm × 38 cm. Fat suppressed T2-weighted turbo spin echo (TSE) sequence was obtained with simultaneous use of respiratory gating with following parameters: TR/TE—6600–8600 ms/84 ms, slice thickness—6 mm, interslice gap—1 mm, matrix—320 × 320, and field of view—38 cm × 38 cm. The DWI (single shot echo planar imaging with simultaneous use of respiratory triggering) was obtained with following parameters: TR/TE—6600–8400 ms/92 ms, slice thickness—6 mm, interslice gap—1 mm, field of view—38 cm × 38 cm, and matrix—320 × 320. The acquisition was done with four *b* values of 0, 100, 500, and 1000 s/mm^2 with diffusion encoding gradient in all three orthogonal directions. DWI sequence was of around 4–5 min. The trace images were obtained separately for all the four *b* values. Imaging software on the imager console automatically generated a pixel-based ADC map. The DCEMR images were obtained using 3D gradient echo FLASH (volume interpolated breath hold examination, VIBE) sequence using following parameters: TR/TE—6600–8400 ms/92 ms, slice thickness—6 mm, interslice gap—1 mm, field of view—38 cm × 38 cm, and matrix—320 × 320. The images were acquired before injecting contrast and after the time period of 30, 70, and 180 s after injecting contrast corresponding to arterial dominant, portal venous, and delayed phase imaging. Gadobenate dimeglumine (multihance) contrast was injected (0.1 mmol/kg of contrast material) through antecubital vein using a power injector at a rate of 2–3 ml/s. Subtraction images were generated automatically on the console by the imager software for every set of post-contrast images for assessing enhancement in nodules that were of high signal intensity on T1-weighted images before injection of gadolinium.

Image Interpretation

The conventional sequences including T1 WI and T2 WI were interpreted for presence of lesion, number of lesions, and for signal characterization of lesion in both the sequences. The DWI and DCEMR images were interpreted separately by two different radiologists. Both of them had more than 10 years of experience in abdominal imaging. The lesions which showed enhancement in hepatic arterial phase with or without washout in delayed images were considered positive in DCEMR for HCC. The lesions which appeared bright on DWI and dark on ADC maps were considered positive in DWI for HCC. On ADC maps, ADC values of the lesion were measured by placing region of interest (ROI) manually within the lesion. At least five ROIs of uniform size of 44 pixels were taken within the lesion and mean ADC value was calculated. While measuring the ADC values, care was taken to place ROI exactly within the part of lesion corresponding to solid enhancing

