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Research Article

To determine sensitivity of diffusion weighted imaging for diagnosis of hepatocellular carcinoma, keeping the dynamic post contrast MRI as gold standard.

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INTRODUCTION:

There is increasing incidence of hepatocellular carcinoma (HCC) worldwide, being the fifth commonest cancer and holds being the second commonest reason of cancer death [1]. It is alarmingly on rise in Pakistan [2, 3]. Multiple risk factors for HCC have been documented worldwide, a few include alcohol, hepatitis B and C viral infection and non-alcoholic fatty liver disease (NAFLD). With current disease load it is crucial to accurately diagnose HCC at the early stage for reducing the morbidity and mortality. Early diagnosis is the rate limiting step in the disease burden. [4] Non-invasive imaging modalities have a fundamental part in the diagnosis of HCC. Ultrasonography (USG) remains the baseline imagining modality. It is extensively used as its screening test. The documented sensitivity of HCC diagnosis through USG is 51%-87% and specificity of 80%-100% [5]. Followed by conclusive enhancement pattern as described in LI-RADS on CT or/and MRI liver dynamic consisting of enhancement appreciated on arterial phase. This shows washout on portal venous and/or delayed phases. This does not requirement histopathological confirmation [6]. In addition to these, promising results are acquired from DWI in adjunct to hepatobiliary contrast study on MRI side by side perfusion imaging and elastography. Such modalities have an important role in staging, surveillance and prognosis of disease, as well as early detection and characterization [7].

Several studies about diagnosis of HCC have reported high sensitivity of DWI combined with contrast enhanced MR. Yet to the best of our literature review only limited studies are available that compares the DWI efficacy alone in diagnosis of HCC against post-contrast dynamic MR. On bases of our clinical experience, we hypothesize that DWI may act as a standalone tool for recognizing HCC lesion in a patient with established cirrhotic liver morphology. The aim of our study is to evaluate DWI performance compared with contrast enhanced T1WI, using later as the standard for reference.

METHODS

This study was performed retrospectively followed approval from Institutional Ethic committee of Medical education and research. All patients with known cirrhotic liver morphology due to hepatitis B or C virus were included in the study. Whereas, any patient with post treated status either through chemoembolization or TACE for HCC were excluded. This resulted in total104 patients with confirmed diagnosis of hepatocellular carcinoma from electronic data base of hospital from July 2018 to October 2020. Fully written informed consents were received and signed from all included patients at the time of history taking in outdoor patient department. At the time of presentation it was ensured that each patient did not have had any previous loco-regional therapy. There were 104 (90 men and 14 female), with age ranging between 39-78 years (mean age of 55.8 years).

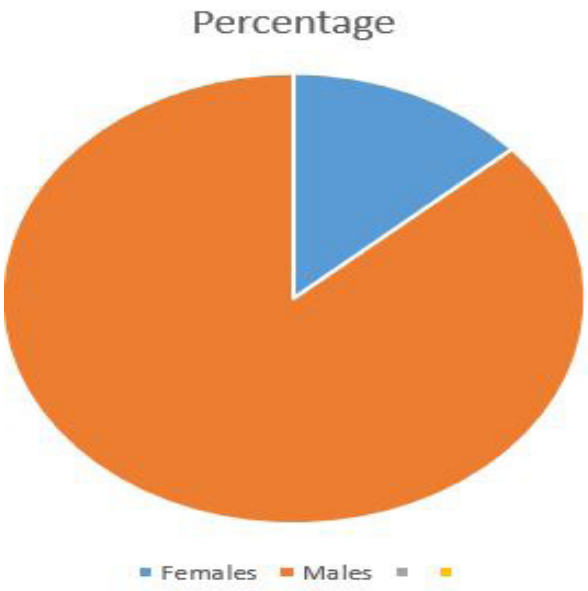

Table 1: Pie chart presentation of gender distribution in study population.

MRI were performed using 1.5 Tesla Titan Toshiba. Examination included non-enhanced T1 and T2 weighted axial and coronal views (out of phase and in-phase images) and axial SPIR weighted sequence and diffusion weighted images of MRI. Post-contrast T1 weighted MRI axial dynamic images were acquired after a bolus of injection of 0.1 mmol/kg body weight of the gadolinium-DTPA at the rate of 2ml/sec, which is flushed using 20 ml of sterile normal saline solution through a power injector. Axial T1 post-contrast images were acquired

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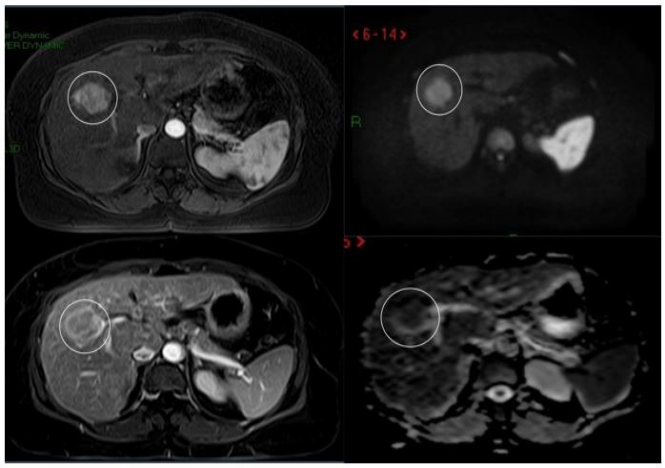
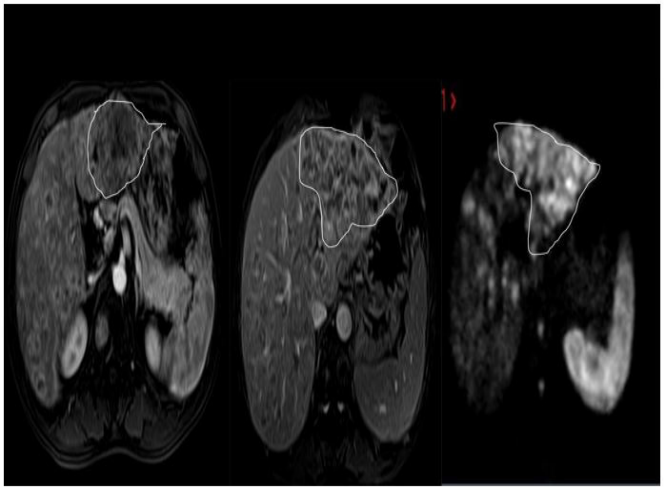
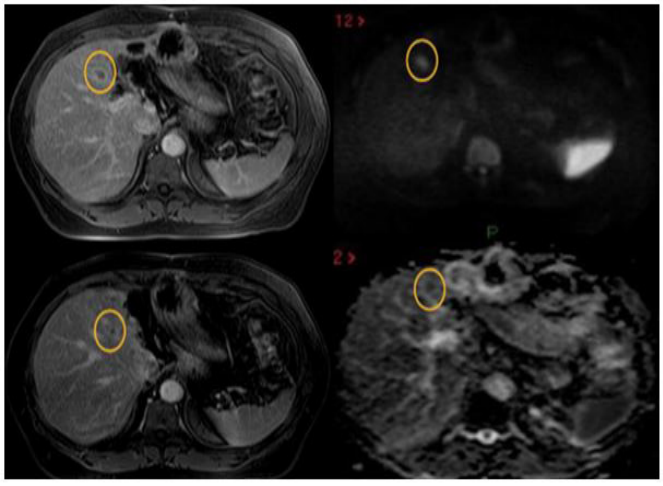
in triphasic manner; included one non-enhanced series then four consecutive post-contrast series consisting early arterial, early arterial phase, portal phase, and a delayed (equilibrium) phase at 25, 60 and 180 seconds were acquired.



Right lobe lesion showing typical enhancement on arterial phase and washout on venous phase MRI. Same lesion showing restricted diffusion on corresponding images



MRI liver dynamic, atypical arterial enhancement pattern in an infiltrative left lobe lesion, with patchy areas of washout on venous phase. Lesion however clearly depicts restricted diffusion and is avidly DWI bright.



Solitary small HCC with avid washout on venous phase images. Small <2cm lesion showing restricted diffusion as shown by white circle.

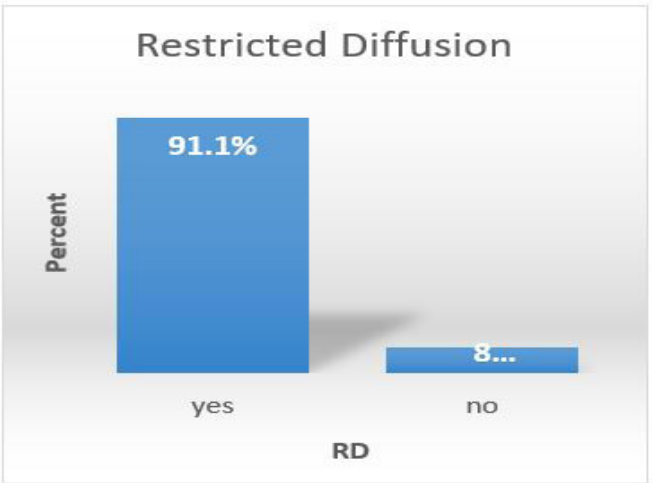
Data was analyzed by two separate radiologists. For the analysis of data, size was measured in longest axial dimension through post-contrast enhanced region of the lesion. Intensity pattern of signal on T1, T2 and fat suppressed sequences were documented. Enhancement pattern through the dynamic enhanced MRI and subtracted images and/or correspondingly showing washout in comparison to the background liver parenchyma on the subsequent phases. Similarly the index lesion was interpreted on diffusion weighted and ADC sequences.

RESULTS

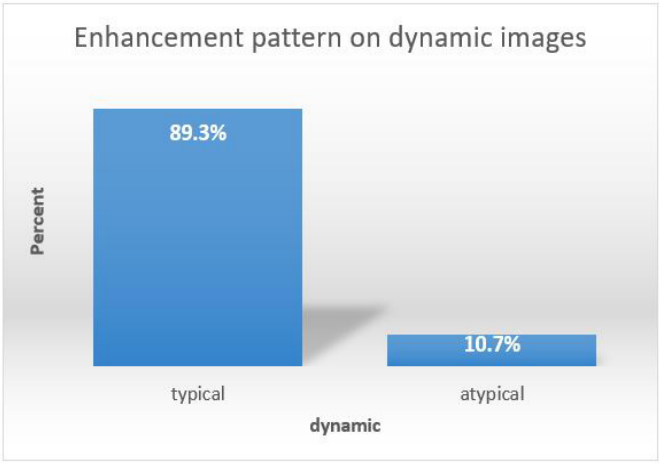
Among our total 104 patients variable number of lesions were seen in each patient. In 26 patients there was one lesion, 16 patients had two lesions and 6 patients had four lesions while numerous lesions were appreciated in 4 patients. In case of multifocal or infiltrative lesions, one most prominent index lesion was take for the study.

The sizes of the lesions were variable, measuring to be from 1-2cm to more than 5 cm in their maximum dimension. Their mean calculated to be 2 cm. In patients having lesions more than one, the most prominent and largest lesion was considered to be the index lesion for the purpose of statistics. On the bases of intensity of signal in each lesion, those being hypointense on T1WI and T2WI were included in the study. Interpretation of lesion on post-contrast MRI showing arterial phase enhancement on post-T1WI followed by washout on venous and delayed phases turned out to be 88.4%; while a few among the included lesions were showing equivocal arterialized enhancement and washout (11.6%). These lesions were then interpreted on DWI sequence as well. Out of total 104 patients, 102 patients were showing homogenous bright signal making it about 91.1%. These lesions were similarly low on ADC.

The data was analyzed using SPSS version 21.0. We calculated the percentage of lesions using various criteria arterialized, venous washout, and atypical arterialized, atypical venous washout in diagnosing HCC. These lesions signal on DWI/ADC for restricted diffusion were calculated which turned out to be 89.3 % (100 patients) showing typical pattern on post-contrast dynamic imaging. Among 104 patients 15 % (8 patients) showed equivocal pattern of enhancement on arterial phase followed by venous phase washout. Restriction diffusion was seen in 102 patients (91.1%) with resultant sensitivity of diffusion weighted imaging alone for diagnosis of HCC measured to be 94 %.



Graph 1: *Sensitivity of diffusion weighted imaging alone for diagnosis of HCC 94 %.*



Graph 2: *Graphical presentation of typical vs atypical enhancement followed by washout pattern on arterial and venous phases.*

DISCUSSION

One of the most common cancers is hepatocellular carcinoma and ranks as second most common cause of cancer death [1, 2]. An early diagnosis of HCC is crucial in order to avail the curative treatment, as they are aggressive tumors with massive metastasis. (8) Early diagnosis with no metastatic spread makes the patient eligible for treatment which offers a good prognosis ranging between 50-70% 5-year survivals. Good prognosis has been documented for those patients who are diagnosed timely at an early stage with no metastasis. This makes them eligible for curative treatments, hence have a good prognosis that ranges between 50–70% with 5-year survival rate [9]. A non-invasive radiological imaging criteria that is used as a gold standard include post contrast enhancement on arterial phase followed by washout on portal venous and/or delayed phases on computed tomography (CT) or magnetic resonance imaging(MRI). (10)

This criterion has limitation in patients with chronic kidney failure, where gadolinium contrast cannot be used as risk of nephrogenic systemic fibrosis and in those with a known allergy to MR contrast. Such cases calls for an additional sequence which does not use contrast and yet provides definitive results.

DWI sequence is progressively used in characterization and detections of liver lesion. This benefit it attributed to echo-planar along with parallel imaging techniques. This characteristic has improved image quality with decrease of several artefacts resulting from bowel peristalsis, breathing and cardiac motion. (11) There are several studies that have reported the significant sensitivity of DWI combined with contrast enhanced MRI in diagnosing HCC. To the top of our awareness and understanding only limited studies are available that compares the efficacy of DWI against contrast enhanced dynamic MR.

We performed our study for the assessment of DWI as a standalone sequence for evaluation and diagnosis of HCC, taking post-contrast dynamic MRI as gold standard. Owing to immense soft tissue resolution and lack of ionizing radiation MRI is playing a crucial role. According to N. Bharwani et al. DWI-MRI is widely used as a standard imaging sequence with the usual non-contrast T1/T2 weighted imaging and post-contrast T1 dynamic for evaluation of liver (12). This is what was introduced in our hospital in 2019, and played a milestone for HCC diagnosis.

In past a study performed by Nasu et al. on 125 surgically resected hypervascular HCCs, which were depicting hyperintense signal in lesions on DWI (13). Similar results were obtained in a study by Piana G et al. which was performed on 91 patients that documented that combination of DWI with the conventional post-contrast MRI enhanced the detection of HCC in comparison to post-contrast alone (14). In similar study, these results were stable in hepatic lesions for size smaller than 2 cm. In this study, 91.1% of HCCs were hyperintense on DWI. This percentage is slightly greater than in earlier studies as stated before in Piana et al., where 82% or 72% of HCC were hyperintense, whereas about 91.2% of arterialized HCC were hyperintense in the study by Nasu et al. (13, 14). Through our study, a higher sensitivity of DWI alone was also detected compared a study by Le Moigne F et al. (15).

In a more recent data analysis of nine studies, showing nearly similar results to ours where sensitivity of DWI was 81% and specificity of 89%. However, contrary to our study this paper documented that DWI in combination with contrast enhanced MRI had a higher sensitivity than that of the DWI alone (16). These studies supported the combination of DWI with CE-DWI, and had certain reservation on DWI alone in detecting HCC.

There are certain studies that mentioned the difficulty in differentiating liver carcinoma from additional firm liver masses like focal nodular hyperplasia, metastasis or adenomas. Preceding studies have cited as well that it may be difficult to differentiate HCC from other solid hepatic lesions like focal nodular hyperplasia (FNH), adenomas, and metastasis by DWI. In a recent paper by Nowicki TK, described that solid hepatic lesions show ADC value that overlaps with that of HCC (17). However the primary study population of our research are patients with either known or high suspicion of HCC with background cirrhotic liver morphology. With such liver morphology possibility of FNH and adenomas is least (18). DWI may be helpful and non-invasive substitute for the diagnosis of HCC in patients with impaired renal function or contrast allergies stopping the use of contrast (19). As presented in this paper, DWI can act as good diagnostic tool in the evaluation of HCC regardless of size.

CONCLUSION

There is a little doubt that DWI has an immense influence in detection of the liver lesion. It is routinely incorporated into the standard liver MRI protocol in many departments across the globe. DWI can act as separate sequence in detection of hepatocellular carcinoma in patients with contraindication to contrast administration. Determining novel non-invasive diagnostic modality to add value and improvement in diagnosis of HCC is challenging, this study will open doors for innovative researches in future. Further larger studies are still needed to establish the value of DWI alone for detecting HCC.

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