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Original Article

Role of dynamic contrast-enhanced and diffusion weighted MRI in evaluation of hepatocellular carcinoma after chemoembolization

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ABSTRACT

Purpose: To assess the role of dynamic contrast- enhanced and diffusion-weighted (DWI) MRI in the evaluation of the response of hepatocellular carcinoma (HCC) after chemoembolization.
Patient & method: 30 patients having 40 HCC lesions underwent transcatheter arterial chemoembolization (TACE). Ages ranged between 41 and 76 years. All examinations were performed using Philips 1.5 Tesla MRI (Achieva). Precontrast T1, T2, Dynamic contrast enhanced and respiratory triggered DWI MR images with (b = 50, 400, 800 mm/s). DWI MRI images and Contrast-enhanced MRI images after TACE are assessed to evaluate post treatment response. DWI was used to create ADC maps and ADC values were calculated looking for a cut off value using the ROC curve.
Results: Dynamic MRI had a sensitivity of 94.1%, a specificity of 95.6%, PPV value of 94.1%, NPV of 95.6% and an overall agreement of 95% compared to 82%, 73.9%, 70%, 85% and 77.5% respectively of DWI MRI. The difference between the malignant residual and well ablated groups' ADC variables was statistically significant P value 0.009.
Conclusion: Dynamic and diffusion MRI complete each other in assessment of HCC response to therapy, especially in those who cannot properly hold their breath that cause degradation of the dynamic MR quality.
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1. Introduction

HCC is the fifth most common cancer in the world. Liver cirrhosis, and hepatitis viral infection, were considered as the major risk factors [1,2].

The curative treatments for HCC are liver resection or transplantation [3]. Other techniques have been used alternatively to surgery for treating the disease, these include TACE, percutaneous microwave coagulation and radiofrequency ablation treatment, these techniques are minimally invasive [4].

TACE affects the tumor to the maximum impact of chemotherapy by selective or super-selective injection of supplying tumor vessels by chemotherapeutic agents and decreasing the tumoral blood supply by the embolization of particles leading to prolongation of the contact between the chemotherapeutic agents and HCC [5].

Parenchymal changes and complications after TACE include the following: Post-embolization syndrome (PES), Arterioportal fistulae (APF), Parenchymal atrophy, Portal vein obstruction, Bile duct injury and acute parenchymal infarction [6].

Following up the effectiveness of TACE with imaging is important in determining the success of TACE and the future therapy of the patient [7].

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging; TACE, transarterial chemoembolization; DWI, diffusion weighted imaging; RECIST, response evaluation criteria in solid tumors; ADC, apparent diffusion coefficient; ROI, region of interest; TN, true negative; TP, true positive; FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; SE, standard error; CI, confidence interval; THRIVE, T1 high resolution isotropic volume examination; SPAIR, SPectral Attenuated Inversion Recovery.

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Non-contrast CT scans assess the introduction of the chemotherapeutic agents into the selected tumor. It may not be easy to evaluate enhancement of contrast in a tumor with partial retention of iodized oil, due to the beam hardening artifacts of iodized oil. However MRI signal is not degraded by iodized oil; therefore, a residual tumor is better detected by MRI [4].

MRI of the liver is considered now the first radiological modality for diseases of the liver [8].

Non-contrast T1- and T2-weighted images show morphological and fluid content changes in addition to fibrosis, while dynamic contrast enhanced MRI demonstrate information on perfusion [9].

Well treated tumors by TACE are commonly replaced by necrosis and decreased interstitial tissue fluid because of the related arterial occlusion. On dynamic contrast-enhanced MRI post-TACE enhancement is either residual tumoral tissue or granulation tissue admixed with necrotic regions. Differentiation depends on the phase of enhancement. Residual malignant tissue gives early arterial enhancement indicating unsuccessful TACE treatment, whereas granulation tissue shows delayed uptake [10].

Also, diffusion can provide information about degree of tumor viability. Necrotic tumors have increased water diffusion and increase ADC values due to cell membrane damage, whereas viable tumor cells have restriction of water diffusion and relatively low ADC [7–11].

2. Patients and methods

2.1. Patients

30 patients having 40 HCC lesions referred to radiology department of Tanta Cancer Center from outpatient clinic of internal medicine and surgery departments who underwent transarterial hepatic chemoembolization over a period of 12 months (December 2015–November 2016). The patients' age ranged between 41 and 76 years (median 58.76); 24patients were males and 6 were females.

2.1.1. Inclusion criteria

Patients with HCC who underwent TACE.

2.1.2. Exclusion criteria

Contraindications to MRI, contraindications to contrast media and liver tumors other than HCC.

2.2. Methods

All cases had been subjected to the following:

- Full clinical assessment.
- Revision of the patient's laboratory investigations including renal function tests (blood urea and serum creatinine).
- Revision of the radiological investigations previously done for the patients.

All patients were scheduled to undergo dynamic MRI and diffusion weighted images within 1 month post TACE to monitor tumor response to TACE and were asked for further for follow-up 3 months later.

MRI protocol includes:

- All cases were performed using Philips 1.5 Tesla MRI (Achieva) scanner.
  (a) Precontrast conventional study includes:
    - Axial T1WIs (TR = 10msec, TE = 4.6msec, flip angle = 15°).
    - Axial T2 WIs (TR = 560msec, TE = 26-28msec, flip angle = 90°).
    - Axial T2 fat suppression (SPAIR) (TR = 560msec, TE = 26-28msec, flip angle = 90°).
    - We used FOV = 315–350 mm, slice thickness = 7 mm, interval = 2 mm for all axial precontrast sequences.
    - Coronal T1 WIs.
    - Coronal T2 WIs.
  (b) DWIs:
    - Diffusion MR images were performed before the dynamic study using respiratory triggering fat-suppressed single shot spin echo-planar sequence.
    - It was obtained by applying b values of 50, 400 and 800 s/mm^2.
    - The acquisition parameters were (TR/TE: 1700/76 ms), matrix 120 × 95, FOV as small as possible, slice thickness 7 mm, Interval 2 mm, scan time 3–6 min.
  (c) Dynamic contrast enhanced study:
    - Dynamic study was done after diffusion study to avoid the effect of contrast agents on ADC value.
    - Dynamic study was performed after bolus injection of 0.1 mmol/kg body weight of Gd-DTPA, flushed with 20 ml of sterile saline solution from the antecubital vein. The injection of contrast and saline was performed manually.
    - Dynamic imaging technique was performed using 3D fat-suppressed T1-weighted gradient echo (THRIVE) sequence.Dynamic series consisted of one pre contrast series and then three successive post contrast series including early arterial, late arterial, and portal phases with 19–21 s intervals. This was followed by delayed phase imaging at 5-min.Patients were examined in end expiration to limit the possibility of image misregistration.
    - Acquisition parameters were flip angle = 10; matrix size = 172x135; field of view = 300–400 mm, slice thickness = 2–3 mm.
  (d) ADC map and ADC value:
    - ADC maps were generated on the workstation. The three b values (50, 400, 800sec/mm^2) were used for ADC calculation.
    - Calculation of the ADC value was an automated process available on the workstation.

All cases were viewed by 2 experienced radiologists in hepatic imaging.

- MR images were analyzed for the following:
  - The morphological features of each lesion were recorded including size, border, signal characteristics at T1 and T2.
  - The enhancement pattern at the dynamic imaging.
  - Signal intensity in diffusion imaging with ADC values using a commercially windows workstation.
  - The region of interest (ROI) used to measure the ADC value was applied as following:
  - The ROI included nearly the entire lesion if it displayed diffuse homogeneous or heterogeneous signal on ADC map.
  - If the lesion had well-defined areas of restriction and other areas of facilitation the ROI was placed on each area separately and two ADC values were calculated.
  - The ADC values were measured three times and the average was taken.
- **Interpretation of the MR image:**
  - The signal of the embolized zone at T1 and T2 was classified as high, low, isointense or heterogeneous.
  - Dynamic study interpretation:

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