The Egyptian Journal of Radiology and Nuclear Medicine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

The Egyptian Journal of Radiology and Nuclear Medicine

journal homepage: www.sciencedirect.com/locate/ejrnm

Original Article

Role of diffusion-weighted magnetic resonance imaging in the evaluation of hepatocellular carcinoma response to transcatheter arterial chemoembolization using drug eluting beads; correlation with dynamic MRI

Mohamed I. Yousef*, Medhat M. Refaat, Mohamed H. Faheem

Department of Radiology, Benha Faculty of Medicine, Egypt

ARTICLE INFO

Article history:
Received 10 March 2017
Accepted 11 May 2017
Available online xxxx

Keywords:
HCC
DW MRI
DCE MRI
DEB TACE

ABSTRACT

Aim: To evaluate accuracy of DWI in evaluating HCC response to DEB TACE and compare the results with DCE MRI.

Material and methods: 42 patients with 59 lesions underwent precontrast abdominal MRI, DWI, ADC map with ADC value measurement and DCE MRI. The qualitative DWI and ADC values were correlated to the DCE MR findings.

Results: Comparing the qualitative DWI findings to DCE MRI, showed sensitivity of 83.9%, specificity of 64.3%, positive predictive value of 72.2%, and negative predictive value of 78.3% and overall accuracy of 74.5%. The measured ADC values showed significant difference (P value <0.05) between the ADC values measured in the active tumoral areas and necrotic areas with no significant difference between areas of active tumoral enhancement in the different groups. ROC analysis for ADC values showed area under curve 0.7 and maximum combined sensitivity and specificity of 79% and 69.6% respectively at cutoff ADC value of 1.395 mm^2/sec.

Conclusion: DWI is useful highly sensitive technique in evaluation of HCC response to DEB TACE, yet it has low specificity related to high number of false positive results preventing using it solely. Also, DWIs is a reliable method in differentiation between active tumor residue/recurrence and benign perilesional enhancement.

1. Introduction

Hepatocellular carcinoma is one of the leading causes of morbidity and mortality world-wide, with an estimated incidence of more than 500,000 new cases per year [1].

The curative treatment regimens such as surgical resection and percutaneous ablation can be applied only to <30% of patients at time of presentation [2]. Randomized controlled trials on patients with intermediate stage unrespectable HCC showed that TACE improves survival among this patients group and can serve as a bridge for liver transplantation [3].

The DEB-TACE showed tendency to cause higher response rates [4], less systemic effects [5] and fewer number of treat meant sets [6] compared with conventional TACE.

In response evaluation criteria in solid tumor (RECIST) system, response of HCC to loco-regional therapy using MRI relies on tumor diameter changes, which is a late finding, while in modified RECIST1.1 system, it relies on presence of tumor necrosis and change in the diameter of the residual enhancement at contrast-enhanced MRI [2]. Therefore, The European Association for the Study of Liver Disease (EASL) has recommended the use of lesion enhancement, rather than change in size, as the standard method to determine treatment response [7].

In 2001, EASL accredited evaluation of tumoral necrosis in response to therapy, by using dynamic contrast-enhanced imaging techniques [8].

MRI has an evolving role in the evaluation of the liver pathologies due to high soft tissue imaging resolution, and the abilities to perform functional studies [9]. In the last decade, DWI of the upper abdomen was a challenging technique due to respiratory motion and long acquisition times. The emerging fast techniques, as parallel imaging, make DWI of the upper abdomen applicable [10].

Peer review under responsibility of The Egyptian Society of Radiology and Nuclear Medicine.

* Corresponding author.
E-mail address: dr-mohamed77@hotmail.com (M.I. Yousef).

https://doi.org/10.1016/j.ejrnm.2017.05.004
0378-603X/

Diffusion weighted MRI has some advantages compared to dynamic MRI. First, contrast medium administration is not required. Second, the examination is obtained in a relatively short time. third, the technique is easy to be repeated, allowing close follow-up during and after tumor treatment. Also, image post-processing is less time consuming compared to dynamic contrast-enhanced MR imaging. At last, ADC value calculation allows easy evaluation of the whole tumor. This is important because of the inhomogeneity that may occur within tumors [11].

Diffusion-weighted imaging began to play a role in oncology field as it reflects the Brownian motion of the water molecules within the tumor, and hence points to its viability. The viable tumor cells have intact membranes that cause restricted diffusion whereas necrotic tumors have increased water diffusion due to disruption of the cell membrane [12]. Also, Luna and Luna recommended ADC calculation as an early functional marker of tumor response to treatment [13].

2. Material and method

The study enrolled 45 patients (38 men and 7 females, age range 38–75 years, mean age 59), including patients proven to have HCC on top of liver cirrhosis secondary to hepatitis C virus and were eligible for TACE. All these patients were diagnosed according to the American association for the Study of Liver Diseases (AASLD) practice guide-lines on the management of HCC [14]. They were candidates for TACE according to Barcelona cancer liver clinic (BCLC) [7]. 38 patients underwent one DEB-TACE set and 7 patients had 2 sets.

Informed consent was obtained from all individual participants included in the study.

2.1. TACE technique

They underwent TACE using Doxorubicin eluting beads (Hepaspheres®; Biosphere-Medical, Paris, France) 30–60 micron impregnated in 50 mg Doxorubicin for 24 h. We used 2.8Fr microcatheter/wire (0.014, 0.016, 0.018) (Renegade Hiflow; Boston scientific, MA, USA) to do as much as possible superselection of the tumoral feeding arteries. The patients are then subjected to DCE MRI and DWI within 3 weeks up to 5 months post DEB-TACE to assess tumor response to treatment (the mean interval between DEB-TACE, and DCE-MRI and DWIS WAS 45 days). The patients were studied prospectively over the period from June 2013 to Decemeber 2014.

3. MR imaging

The study was conducted using one MRI machine (Philips Achieva 1.5 Tesla SE, 16 channels) equipped with phase array torso surface coil. First, conventional magnetic resonance imaging was performed using axial T1WIs (in and out of phase) (TR = 10 msec, TE = 4.6 msec, flip angle = 15°), axial T2 WIs (TR = 1000 msec, TE = 80 msec, flip angle = 90°) and axial T2 fat suppression (SPAIR) (TR = 1000 msec, TE = 80 msec, flip angle = 90°) FOV = 300–350 m m, slice thickness = 7 mm, interval = 2 mm. DWIs were performed before the dynamic study using respiratory triggering fat-suppressed single shot echoplanar sequence that combined the diffusion gradients along the section selection, phase encoding, and frequency encoding directions and data acquisition by echo planar imaging read out, obtained by applying b values of 0, 20, 400 and 800 s/mm^2 and acquisition parameters (TR/TE: 1700/76 msec), matrix 120×95, FOV as small as possible, slice thickness10mm, Interval 2 mm, scan time 3–6 min. DCE study (acquisition parameters TR/TE10/4.6msec, flip angle 15°, matrix size 172×163, FOV 300–350 mm, slice thickness 7 mm, interval 2 mm) done using 3D fat suppressed T1-weighted gradient echo sequence (THRIVE T1 high resolution isotropic volume examination) after bolus injection of 0.1 mmol/kg body weight of Gadolinium –DTPA/Gadopente tatedimeglumine (magnavist; Schering, Berlin, Germany) using an automatic injector at rate of 2 ml/s, consisting of precontrast series followed by 5 successive phases timed 14, 30, 50, 180 and 300 ss post contrast administration. Pixel- based ADC maps were generated on the work station (Philips Extended MR workspace) using four b values for ADC calculation.

4. Standard of reference

It was difficult to obtain pathologic confirmation because most of these patients are not candidates for surgery, in addition biopsy is an invasive technique and may result in sampling errors as residual lesions are mostly small nodules, and so according to the enhancement pattern in the dynamic study, we categorized the lesions into 4 groups including: "***complete response group***" showing total necrosis of the lesion with no signs of residual viability, "***partial nodular enhancement group***" with partial nodular (measurable) residual arterial enhancement followed by washout of contrast in the later phases, "***heterogeneous enhancement group***" where heterogeneous (non measurable) residual arterial enhancement of the lesion intermingled with areas of necrosis followed by contrast wash out in the later phases, "***diffuse enhancement group***" showing still complete diffuse arterial enhancement with no areas of necrosis.

According to Hwang et al. The "***benign perilesional enhancement***" referred to the uniform rind like enhancement and the perilesional enhancement that persist in the delayed phase [15]. The benign perilesional enhancement was found in 13 lesions and follow up studies were done after 3–6 months to ensure their benign nature by lack of progression in the follow up study.

The signal intensity of the lesions on the DW images and ADC map were sorted into three types including: "***restricted diffusion***" identified by sustained hyperintensity in the high b value DW images combined with dark signal on ADC map, "***facilitated diffusion***" identified by dark signal on high b value DWIs combined with high signal on ADC map, and "***Uncertain signal***" identified by moderate hyperintensity on DWIs with isointensity on ADC map, or lesions displaying heterogeneous signal on DWIs and ADC map.

The restricted diffusion was considered true positive when it was related to residual tumor enhancement on the DCE, and considered false positive when it was related to necrotic tissue or benign perilesional enhancement. The facilitated diffusion is considered true negative when it was correlated to necrotic tissue or benign perilesional enhancement and considered false negative when it is correlated to the residual tumor enhancement.

ADC value was calculated with ROI applied to the areas corresponding to tumoral enhancement and those areas corresponding to necrosis. In the heterogeneous enhancement group, the ROI was applied to the whole lesion. In the partial nodular enhancement group, ADC calculation is done retrospectively by applying the ROI to the areas related to the tumoral enhancement and to the areas related to the necrosis on the DCE MRI images. ADC value was also calculated from the area of benign perilesional enhancement detected in the dynamic study.

5. Data analysis

Data management and statistical analysis were performed using: